Damaging Sex: Hormones as a point of convergence in the construction of medical bodies

Emily Mauldon

July, 2000

A thesis submitted for the degree of Doctor of Philosophy of the Australian National University

Except where indicated otherwise, this thesis is original work.

Emily Mauldon

Acknowledgments

I warmly acknowledge the encouragement, support and friendship of my supervisors, Dr Dorothy Broom, Dr Anni Dugdale, Dr Kevin White and, in the early years, Dr David Legge. In particular, I am grateful to Dorothy and Anni, a formidable and entertaining duo, who I enjoyed working with immensely. I have learnt a great deal from the staff and students at the National Centre for Epidemiology and Population Health who have provided a stimulating collegial environment. Special thanks to Professor Bob Douglas for always making time to listen, and Dr Cathy Banwell and Dr Andrea Whittaker for their consistent friendship and interest in my work. I am also indebted to my parents, Roger and Willa Mauldon, for academic and personal help during my time as a graduate student. Finally, thanks to James, Ada and Odette for giving me a reason to stay sane and keep smiling.

ABSTRACT

Normative modernist accounts of the construction of scientific medical knowledge, beliefs and practices disavow the part played by social variables in the constitution of medicine as a discipline. Although social factors are recognised as an integral part of the policy and research agenda of biomedicine, beliefs about scientific medical knowledge hold that when medical research (and its subsequent application) is carried out in a rigorous manner it will remain free from the impact of extraneous social influences.

Despite critiques within history, philosophy and sociology, this modernist approach to scientific knowledge continues to underpin medical research and policy practices. This thesis explores the continuing commitment to the notion of 'truth' within medicine. An explanation of how accounts of the history of particular beliefs and technologies are made durable and how they function helps explain the persistence of this commitment to scientific realism in medicine. Contemporary biomedical histories of 'evidence-based practice' are analysed through two case studies, each of which centres on entities generally considered to be 'real': breast cancer and prostate cancer.

Because randomised controlled trials (RCTs) are understood to be the 'gold standard' in the production of scientific medical knowledge, the case studies focus on RCTs: involving first, the use of tamoxifen in the prevention of breast cancer and second, hormonal discourses in the conceptualisation and treatment of prostate cancer. A major focus of the thesis is a sociological account of how RCTs' operate in relation to the traditional scientific method story, and how this ideal connects with practice as described within medical literature. The tensions and contradictions between the belief systems and rhetoric which surround clinical trials, and the ways in which they are

practised, open fertile disjunctions from which to tease out questions about RCTs epistemological and political foundations. The case studies are developed by analysing published medical and sociological commentaries and policy documents.

A belief in a stable, fixed, and ultimately 'knowable' biology is necessary to sustain a commitment to RCTs as they seek to map and codify a universalisable body. RCTs construct female and male bodies in different ways and to different political ends. The socially unstable nature of the body is explored through a blending of poststructural and postmodern critiques of the body with the emergence of discourses and practices relating to sex hormones.

Finally, the thesis deals with how ideas about the sex/gender distinction are represented both ideologically and practically within medicine. Research on prostate cancer is contrasted with the breast cancer case study to illustrate some of the differences and inconsistencies in the way medicine treats and conceptualises women and men. These inconsistencies emphasise the need for a continued feminist analysis of the impact of sexual politics on the provision of services to both women and men in order to develop strategies for positive intervention in the research and policy arenas.

Overall the thesis develops an account of the complex ways in which social values are woven through the intellectual and material practices of medicine. Tracing how seemingly distinct areas within medicine are linked through beliefs and practices about scientific, biological, and sexual knowledge provides strategies for influencing the perceived truth and stability of these constructs.

TABLE OF CONTENTS

CHAPTER 1

Framing the science of medicine and a sociology of medical knowledge

This is a study of the legitimation of knowledge claims within medicine and the consequences of that legitimation for the way medicine impacts on society. The pages that follow tell a story about science as it operates in late twentieth century medicine and about the authority of the randomised controlled clinical trial (RCT) as the exemplar of scientific medical practice. I explore the relation between science and beliefs about the human body, and how understandings of human bodies affect sexual and social equity. My argument is that there are webs of beliefs, practices, and material phenomena that shape our experience of the world, and it is only through the interaction of these forces that we are able to know the world or to speculate about its nature. Beginning with an analysis of RCTs, I develop an account of the way these webs construct knowledge of biology and experiences of the lived body.

This first chapter identifies the historical and theoretical starting points that frame the terms of my inquiry. My sociological training inclines me to give primacy to human accounts of the world. Humans exist within a physical world that both constrains and enables their actions, but the point at which the materiality of the world ends and sociality begins is impossible to ascertain. My work is less concerned with ontological and epistemological questions about the boundary between natural and social objects and knowledge, than it is with the socio-political construction of a division between the two and the implications this has for the expression and maintenance of any such boundary. In order to develop a

throughgoing account of the practice of RCTs I have drawn on literature from feminist critiques of science, the sociology of scientific knowledge (SSK) and literature on the making of the body. This chapter is made up of four sections, beginning with an account of 'commonsense' beliefs about science and medicine. These beliefs are significant because they feed into accounts of the sexed body as biologically fixed and historically inflexible and of science as a privileged means of interpreting this body. They articulate a position from which I want to distinguish myself. The remaining three sections discuss the contributions SSK, feminist critiques of science and post-structuralist accounts of the body have to offer for a sociological critique of randomised controlled trials.

The commonsense view of science and scientific experiment

Of immediate importance for each of the theoretical perspectives I draw upon is the phenomenon of science. 'Science' is an exceptionally powerful force in modern society. Infinitely complex, 'science' is at once a metaphysics, an ideology, an organising principle and justification for numerous material social institutions, as well as a wide range of specific cultural practices. Science is revered as a special and reliable form of knowledge. Pinning down and defining the nature of the multiple enterprises that are 'science' has spawned commentaries as diverse as science itself. Within these commentaries one can identify a 'commonsense' or 'received' view of science. This is the dominant ideological view, the story that science tells about itself, the public face of science, the description that most scientists, politicians and policy makers mobilise in their attempts to order society.

According to this standard view, science is an intellectual and practical system for ascertaining reliable factual knowledge about a natural world. The task of science is to provide an accurate account of the objects, processes and relationships

occurring in the natural world. When scientific knowledge is valid, it systematically reveals and describes the true character of this world (Mulkay, 1979: 19-20). Traditional accounts of scientific knowledge rely heavily on the assumption that the world science seeks to describe is governed by universal and stable a priori physical laws. Science is the project which strives to give an account of these laws and the way they govern the material relationships which make up the world. These laws cannot be influenced by the preferences or desires of an observer but they can be brought to light by the methodologies of objective inquiry, the best representative of which is the scientific experiment (Kuhn, 1970). Although the world is constantly in flux the basic universal regularities represent trans-historical, trans-geographical truths. 'Progress' in science (and scientific medicine) may result in a degree of instability in the expression of these natural laws as new problems disrupt existing theoretical assumptions however this is considered healthy as it indicates a movement towards a greater degree of accuracy in scientific representation of the world (Mulkay, 1979: 29).

The universal laws governing the world can be uncovered by evidence generated through unbiased, detached observation which allows scientists to build a body of theoretical knowledge which explains the observations. To paraphrase Fleck, 'factual' knowledge is supposed to be distinguishable from transient theories because it is definite, permanent, and independent of any subjective interpretation by scientists (Fleck, 1979: xxvii). The authority of scientific knowledge rests on the belief that science has evolved stringent criteria through which empirical knowledge claims and the accuracy of their representation of phenomena are tested. These criteria are embodied in the 'scientific method': a single and transferable set of practices which capture the directness of an encounter between an observer and nature, resulting in the elimination of potential bias on the part of

the investigator and the production of objective truths about the world. The standard commonsense view of scientific knowledge assumes that the rules of method govern scientific experiment in a straightforward way, resulting in a fairly predictable pattern in the growth of knowledge. The most widely known philosophical account justifying this view is Popper's notion of falsificationism (Popper, 1959; Popper, 1963). Merton's influential sociological account of the institutions of science also legitimates the trust placed in scientific knowledge as true knowledge (Merton, 1973).

According to the story of scientific method, 'progess' within science occurs when some novel or unusual claim is identified within the scientific literature or through the workings of scientific practitioners. While trying to solve this puzzle, theoretical deductions are made which are tested against the existing corpus of knowledge using observation and experiment. Although the story of scientific method recognises the necessity of adhering to discipline-specific beliefs and practices when actually 'doing science', at its core it holds that the value of the scientific method is self-evident and the rules for practising the scientific method can be followed by almost anyone. Consequently, it is supposed to be an egalitarian way of generating knowledge:

> [a] reliable observation is one which any individual with normal powers of perception might make. An acceptable law or theory is one which any individual with normal powers of reasoning might justify. Ideally, as it is generally perceived, the whole of science should rest upon such individual acts of perception and justification. And it should so rest because science is then based upon reason and experience alone…" (Barnes, 1985: 80-81).

Science is an intellectual pursuit about which people can be 'enlightened', as the rules by which scientific method operate are straightforward, logical and rational:

> It is a form of knowledge which can be accepted by anyone in a society of equal individuals, out of deference to nothing more than his or her own powers of perception and inference (Barnes, 1985: 81).

More than simply providing tools for generating knowledge, the scientific experiment provides an ideological model for society. In the open minded, disinterested individual, the impartial observation of the natural, carried out in accordance with universal standards of rational thought, will produce unbiased and accurate accounts about the world, and thus a reliable guide to its governance.

One essential component of this scientistic model of society is the belief that the reliability of natural rules (observation statements and theoretical innovations) can be tested using practices prescribed by the rules of scientific method. In other words, should a researcher or research group produce findings which challenge communal expectations, then that result ought be repeatable by others. In practice the act of replicating an experiment is fraught with messy contingencies, but a commitment to the principle that experimental results can be replicated remains "the touchstone of common sense philosophy of science" (Collins, 1985: 18-19). However, while scientists will invoke replicability as a reason for accepting scientific change, they are rarely sufficiently motivated to implement this principle and replicate earlier work as no professional advantages arise from doing so, unless they are seeking to disrupt an accepted theory. Thus the axiom of replicability is more often a demarcation criterion (objective knowledge claims must in principle be susceptible to replication) rather than a matter of practice (Collins, 1985: chapters 1 and 2).

The ethos and ideology of science extend well beyond attempts to account for the physical world: they have become a central feature of our cultural fabric, and the depth of communal commitments to the scientific rationale indicates the extent to which they are now entrenched as an authoritative way of interpreting the world around us. Rhetoric about adherence to scientific method has become a powerful rationalisation for social decision making. The strength of this cultural commitment awards science, and thereby 'scientific medicine', special significance in determining the ontological status of phenomena. The subjects of science and scientific medicine are assumed to be pre-existing elements of the natural world.

Modern western medicine justifies itself largely through its claims to a cognitive foundation within science (Bates & Lapsley, 1985:181). This cognitive foundation is made to work through the techniques of different types of clinical trials, of which the RCT is considered the most valuable because it produces the most scientifically rigorous outcomes (Richards, 1991: 2). The rise of biomedicine during the nineteenth and twentieth centuries has been accompanied by an increasing emphasis on the importance of scientific investigation as a means of arriving at empirically substantiated, generalisable and transferable solutions to medical problems. Like science generally, the scientific component of medicine is supposed to eliminate any prejudice which may result from the interests of practitioners or patients involved with a medical experiment, and should prevent external economic or political factors impacting on the outcome of the experiment (Nelkin, 1987: 283-84). As a discipline, medicine is practised by experts who, through their training in the methods of science, are able to remain emotionally and morally detached while dealing with their patients. Objectivity in assessing contending medical claims and treating patients is seen as beneficial and necessary for ensuring that optimal results are achieved.

In popular accounts of scientific method, representations of actual scientific work are sanitised or escape mention entirely while philosophical questions, such as the logic of scientific justification or confirmation, become the focus of attention. Theoretical claims are abstracted from the context where they are produced, which results in simple linear histories of 'ideas', and to a lesser extent 'practices', being put forward when accounting for the growth of science. Recognition of the everyday work of scientists is rarely included in such accounts, and when it is acknowledged it is usually for the purposes of establishing epistemic warrant of theoretical claims and is reduced to descriptions of data gathering and experimental hypothesis testing. But when undertaking scientific investigation the problems surrounding experiment are not simply reducible to epistemological and ontological questions about adherence to method. Instead, as the following discussions on the sociology of knowledge and feminist critiques of science and technology illustrate, scientific work involves the everyday practicalities which make up the relationships, be they personal, institutional or technological, within which scientists live their lives.

Tools from the sociology of scientific knowledge (SSK)

In western intellectual traditions the distinction between 'knowledge' and 'belief' usually holds that 'knowledge' is that which can rightfully be considered credible and trustworthy whereas 'beliefs' belong to small groups or individuals and do not warrant acceptance in the wider society (Barnes, 1990: 60). Because the scientific method is seen as ensuring that what counts as scientific knowledge is determined by nature, the sociology of science was traditionally relegated to explaining the persistence of false belief. The sociology of scientific knowledge (SSK), however, holds that the making of all knowledge, including science, is amenable to

sociological investigation. In other words, what comes to count as knowledge is a product of its social context. Despite the historical tendency to assume that scientific and technical knowledge could be exempt from sociological investigations of the kind applied to customary belief, researchers have been producing empirical case-studies since the mid 1960s which demonstrate that there are no a priori epistemological grounds for excluding science from a sociology of knowledge. The epistemological privilege once awarded to science obstructed the development of sociological critique, but over the last three decades the limitations imposed by the old epistemology have weakened and sociologists have extended and modified the work of philosophers and historians so as to produce a robust sociology of scientific knowledge (Mulkay, 1979:2).

Techniques for 'doing' sociology of scientific knowledge are varied. One possible approach articulated by David Bloor is the 'strong program'. Bloor argues that sociological analysis of science should develop a causal explanation for the beliefs and actions of scientists which exhibits the following characteristics; it should be impartial with regard to the perceived 'truth' or 'falsity' of the knowledge in question; it should develop a symmetrical analysis inasmuch as the same explanatory criteria should be used to explain both true and false knowledge; and it should reflexively apply its analysis to its own methods (Bloor, 1976: chapter 1). When sociologists ask the question 'What is a scientific experiment?' their answers will involve examining historical and social issues concerning the systems within and through which experiments occur. The practicalities of how an experiment is performed, the means by which experiments can be said to produce matters of fact, the relationships between experimental facts and explanatory constructs, and the criteria and processes by which the success or failure of an experiment is determined are the subject matter for a sociology of experiment. The

answers which emerge from addressing these issues provide a perspective on why experiments are considered to be a privileged means of generating consensually agreed knowledge and the commitment to doing experiments as a means of arriving at scientific truth that is radically different from the perspective operating in traditional philosophical and historical accounts of science. According to Bloor's principle of symmetry, questions about experimentation can also provide insights into whether or not there are other possible means for constructing robust truths about the world.

In *Leviathan and the Air Pump* Shapin and Schaffer develop historical answers to questions about the nature of scientific experiment (Shapin & Schaffer, 1985). Approaching social analysis from the position of a cultural stranger allows one to query the self-evident methods which that culture employs. In the history of science, as in contemporary sociology and politics, the successes of the experimental programs are commonly treated as their own explanation. That they stand as the pinnacle of the legitimation of everyday cultural practices is not seen as problematic (Shapin & Schaffer, 1985: 5-6).

Sociology of experiment, including Shapin and Schaffer's treatment of Boyle's experimental method, stresses the significance of convention, practical agreement, and of the manual labour of science as productive forces. Such qualities are not usually recognised as significant in the generation of experimental knowledge. By taking this approach Shapin and Schaffer transform the characteristics generally awarded to scientific knowledge, features such as 'truth', 'adequacy' and 'objectivity', into categories of inquiry (Shapin & Schaffer, 1985: 13-14). In my work I follow their lead by looking at claims about scientific method as part of the activity of clinical practice. For example, how are experiments carried out in

clinical medicine? How do experimental findings become constituted as facts? What kinds of criteria are used for judging the success or failure of an experiment and how do they vary across specialities and across time? How, and to what extent, are clinical experiments actually replicated, and what enables replication to take place? Are there hierarchies of medical experiments and knowledges and, if so, on what grounds are these hierarchies constructed?

'Scientific experiment' is a principle around which practioners can consolidate patterns of activity in the everyday practical 'doing' of science and thereby naturalise specific forms of social organisation and specific interactions within the scientific community. For SSK, disputes over scientific method are disputes over different models of action and different practices for organising scientific workers to achieve practical outcomes. Consequently, solving the problems of knowledge becomes a matter of solving the problems of social order, and different practical solutions to the problems of social order involve distinct solutions to the problems of knowledge (Shapin & Schaffer, 1985: 15).

Feminism, Science and Technology

Explicitly feminist critiques of science, technology and medicine have their historical origins in second wave feminism and the increased interest this brought to investigating women's position within society (Wajcman, 1991). Women's experiences at the hands of patriarchal medical professionals, as those at the receiving end of medical knowledge and technologies within clinical practice, provided the catalyst for the initial feminist critiques of medical science. Once feminist attention was directed toward the concerns women raised, the difficulty of reconciling the rhetoric of science with women's lived experiences became apparent. Women's exclusion from and marginalisation within science and

medicine highlighted the structural obstacles women faced in gaining access to professional employment. This posed substantive problems for the social neutrality these professions claimed for themselves (Ehrenreich & English, 1976; Fee, 1986; Rose, 1983). Feminist scholars drew out evidence of women's limited access to scientific jobs and of the relegation of women to low status positions within the profession. The startling inequities which were revealed became levers for policy reform and provided a focus for further research on gender within the professions. Although this work took place in an intellectual and political climate where the supposed impartiality and disinterestedness of science was coming under increasing scrutiny (for example through the work of the radical science movement) mainstream social sciences did not question the relationship between gender and science (Wajcman, 1991). Since the first feminist engagement with science, technology and medicine, scholarship has evolved and fractured and there are now a diverse range of sometimes contradictory approaches available for feminist researchers. Finding a trait which unifies these approaches can be difficult, but perhaps the single most consolidating feature of feminist engagement with science and technology is a recognition of the partial perspectives offered by mainstream science and an acknowledgment that this detrimentally affects the quality of women's lives.

One useful approach to understanding feminist critiques of science, technology and medicine is that developed by Sandra Harding in *The Science Question in Feminism* (Harding, 1986). Harding develops a schema identifying 'feminist empiricism' and 'standpoint feminism' against which she contrasts moves towards a postmodern and social constructivist feminism. Although published nearly fifteen years ago Hardings' commentary continues to provide a useful way of ordering the diversity of feminist critiques. The analysis which focuses primarily

on the gendered barriers to women's equal participation and the reclaiming of their histories within the professions contributes to the project of 'feminist empiricism' (Harding, 1986). Works such as Margaret Rossiters' *Women Scientists in America* (Rossiter, 1982) (which focuses on women's struggles to enter the sciences) describe the gender biases within the sciences as resulting from social factors which are not related to the methodological norms of scientific inquiry. According to feminist empiricism, liberatory social movements, such as feminism, may unsettle social order and thereby remove the old veils which obscure clear knowledge and observation. Feminist engagement with science produces the opportunity for broadening the perspective of science as the increased numbers of women scientists are more likely than their male colleagues to notice science's andocentric bias (Harding, 1986: 25).

Harding identifies the way feminist criticisms of science shifted from asking the 'woman question in science' to asking the more radical 'science question in feminism'. Instead of focusing solely on investigating the marginalisation of women within the sciences and seeking to find ways that woman can be more equitably treated within and by science (the primary focus of feminist empiricism), feminist scholarship turned its attention to ask whether or how a science which seems to be so patriarchal in its constitution and social applications could be used for emancipatory ends (Harding, 1986). Close attention was paid to the gendered methodologies and practices of science and their results for both knowledge production and social implementation of science (Keller, 1983).

The response of feminist empiricism to the epistemological and structural gendered inequities of science appears to leave the methodological norms of science unchallenged. For those interested in doing or using science, this is an

appealing form of critique because it debates the meanings and products of science within terms that maintain a commitment to the standard view of science. Although feminist empiricism offers a subtle subversion of traditional empiricism by drawing attention to the identity of the scientific inquirer, it is a small shift away from the modernist project. It is, however, a useful shift and has provided ammunition for social movements that call for an increase in the objectivity of science by pointing out that the norms of science as they have been practised are often at odds with their philosophical reconstruction (Harding, 1986: 25). Highlighting the importance of the scientific inquirer, however, significantly subverts the modernist project by emphasising the partial perspective of a patriarchal science, and feminist insistence on the potential contributions women scientists can make implies there may be something unique about the standpoint of women as a category.

Feminist standpoint theory was developed from the insights of Hegel, Marx and others, in an attempt to establish an explanation for the authority of feminism, to identify those for whom it speaks and to throw light on "the forces of oppression and exploitation it contests" (Hennessy, 1993: 67). A 'standpoint' is a social location which is created by, and in turn helps create, factors such as prevailing epistemologies, power structures and the distribution of resources. Attending to the complex ways these factors influence women's lives provides the basis for articulating a feminist reality; a reality that captures the activities, interests and values of women yet is self-consciously a product of historical and social conditions. In this way women's experience becomes an empirically grounded basis for feminist authority. Central to the engagement of standpoint feminists with science are attempts to reform knowledge and practice by challenging the andocentrism of current science and by developing scientific explanations which

improve the living conditions and social opportunities available to women. As with feminist empiricism, standpoint feminism has developed as a strategy for justifying scientific projects, and it maintains a commitment to the emancipatory possibilities of science (Harding, 1990: 83).

The most commonly cited problem of standpoint feminism is the way it treats the experiences of women as empirically valid reference points across time and culture, thereby erasing much of the specificity which gives them meaning. As a critical theory, standpoint feminism has been charged with homogenising and universalising women's experiences as they are mediated by feminist interests to form a foundation of feminist knowledge. In particular, the analytic primacy awarded to gender in Anglo-American critical feminism inscribes female and feminist subjectivity within the framework of the racist imperialism and empiricism of traditional masculine European epistemology (Hennessy, 1993: 69, Haraway, 1988).

In contrast to feminist empiricism and standpoint feminism, both of which are positioned within the modernist project (despite providing fundamental challenges to it), feminist postmodernism and social constructionism require a more radical questioning of the nature of science. By claiming that the very criteria which demarcate categories such as science, myth, fact or superstition, are internal to the intellectual conventions of modernism and cannot be justified unless those conventions are invoked, feminist postmodernism and social constructionism challenge the boundary between the natural and social order. Further, they hold that the development, deployment and extension of these criteria of demarcation into social life should be interpreted as indicating the growth of particular "regimes

of power" (Nicholson, 1990: 4). The writings of Donna Haraway provide a case in point.

Haraway's early work investigating the science of primatology supplies an impressive case study detailing the numerous actors and influences involved in the production of scientific narratives. Haraway demonstrates that these actors and influences extend well beyond those outlined in traditional accounts of the growth of scientific knowledge by tracing the effects of phenomenon as diverse as monopoly capitalism, fashions in taxidermy, the effects of colonialism and a specific fictional portrayal of a Pliocene woman (Haraway, 1989). In particular, she uses primatology to question the ordering of difference which constitutes the boundaries between the natural and social worlds. Science for Haraway is a process of storytelling with many 'tellers and hearers' whose presence may or may not be discernible, but whose various stories function to produce scientific reality (Haraway, 1989: 8). Constructed as the most 'human' of creatures within the animal world, 'primates' inhabit the boundary between nature and culture. The bodies of primates can be read as 'maps of power' which reveal the political, historical and cultural discourses through which primates' difference from human kind and other animals have been contested and ordered (Haraway, 1989: 10).

Through the metaphor of the cyborg Haraway to reiterates her insistence on the social and cultural nature of the natural sciences (Haraway, 1991; Haraway 1997). She writes:

> The cyborg is a cybernetic organism, a fusion of the organic and the technological forged in particular, historical, cultural practices. Cyborges are not about the Machine and the Human, as if such Things and Subjects universally existed. Instead, cyborgs are about specific historical machines and people in interaction that often turns out to be painfully counterintuitive for the analyst of technoscience (Haraway, 1997: 51).

The point of the cyborg for Haraway is that it demands a blurring of the boundaries of organic and technological, foregrounding the indebtedness of each to the other and the impossibility and futility of attempting to divide the two. Instead, her interest lies in exploring and bringing to light the competing narratives which constitute any particular instance of technoscience.

The postmodern focus on difference, fragmentation of identity, and the importance of language for constructing meaning and regimes of power has been criticised as potentially neutering feminism's ability to function as a political project (see for example; McNay, 1992: Introduction). If the category 'women' is reduced to an infinitely fragmented array of rhetorical difference, how can it provide a unifying entity around which to focus political action?

The attention this thesis pays to social and historical aspects of legitimation in medical experiment locates my work within the social constructivist and postmodern critique of science; however the ongoing tensions and ambivalences between various feminist critiques of science are themselves also important. Each critique has specific strengths and weaknesses. As Harding points out, the tensions between them reflect the different, and sometimes contradictory, political and

theoretical needs of women (Harding, 1990: 86). If the challenge, as Haraway puts it, is to simultaneously account for the 'radical historical contingency' of science and maintain a commitment to faithful accounts of the world (Haraway, 1988: 579), then a range of strategies for engaging with the material conditions of women's lives are needed.

The Medical Body

The final analytic tool I will employ is drawn from the literature that deals with how human bodies are conceptualised. According to medical science there is a biological body which, with minor variation, transcends history and geographical location. This body is a natural entity which is open to scientific codification and manipulation in straightforward and unproblematic ways. While the human body may be infinitely complex and as yet not fully understood, it is a stable material object whose intricacies are waiting to be unveiled when the right innovative researchers or scientific techniques come along. However, scholars from the humanities and social sciences have sought to demonstrate that human bodies are the products of specific histories, that they have been quite different entities throughout the ages and across cultures and that these differences have affected experiences of the lived body.

In many ways literature on the construction of the body is a logical extension of critiques of science and technology. Science and technology studies problematise 'natural objects' and causal chains that link nature and society, and the critiques of science outlined above pose as many problems for a constitution of the human body as they do for the air pump or the feminist scientist. The human body is a rich repository of meaning. Perhaps more than any other object, it sits on the boundary between the natural and the social world and becomes the marker and

mediator of social and scientific knowledge. The body is a person's most immediate reality. Its accessibility has allowed it to become a formidable part of the interdisciplinarity currently flourishing in the humanities and social sciences. Consequently, writers concerned with the body provide a way to traverse the treacherous terrain of 'sex' and 'gender' and 'science' and, for my purposes, of linking breast cancer and prostate cancer as sites of material, metaphorical and cultural study. Throughout the thesis I will return to and elaborate on the theme of the construction of the body through the rules and practices of cultural life.

Recent developments in social theorising about the body owe a substantial debt to the works of Michel Foucault. For Foucault, the body is radically contingent on the exercise of social power, both as it exists at any given time, and as it has operated throughout history. In particular, he was interested in the production of bodies and their regulation and representation through the various processes of disciplinary surveillance (Turner, 1997: xv). These processes include the exercise of legal and medical power, and social and self discipline through the constraint of desire and morality according to the mandate of the Church (Foucault, 1977; Foucault, 1980). As systems of legal, medical and moral authority change throughout history so too do the ways in which they inscribe bodies. The body is a site of continual struggle between competing forces within society (such as the state, the Church and the medical profession), and is thoroughly imprinted by the histories created as these forces strive to impose their own ideal order (McNay, 1992: 13-16). Foucault sees the way in which the forces in history act upon the body as uncontainable within a totalising historical narrative with the result that the human body becomes 'radically anti-essentialist' (McNay, 1992: 15). In this way he is methodologically aligned with scholars such as Haraway for whom

history is at once a way of understanding the creation of social order and always open to interpretation.

The influence of Foucault has been enormous. His insistence that the body is the product of the prevailing forces of history has enriched feminist critiques of biological essentialism by articulating a way of understanding the body as a material phenomenon without assuming that materiality is biologically fixed. At the same time, however, his own work pays little attention to the gendered nature or consequences of the disciplinary techniques he investigates (McNay, 1992: Introduction, Chapter 1). The impact of Foucault's methods and critical approaches to history, the body and the formation of sexuality, can also be seen in subsequent historical analysis of gender and sexuality (Gallagher & Laqueur, 1987; Laqueur, 1987; Laqueur, 1990) and in the study of the relationship between women and medicine (Martin, 1987; Martin, 1996, see also Turner, 1997).

The ways in which the human body have been understood and represented have changed dramatically across different historical epochs. According to Gallagher and Laqueur this has resulted in dramatically different experiences of the lived body as it is "brought into being within widely dissimilar material cultures, subjected to various technologies and means of control, and incorporated into different rhythms of production and consumption, pleasure and pain" (Gallagher & Laqueur, 1987: vii). In particular, Laqueur argues that a dramatic change occurred in representations and understandings of biology during the eighteenth and early nineteenth centuries (Laqueur, 1990). This change, which can be seen in representations of female biology and sexuality, was attributed to increased interest in and sophistication of the techniques of science. However Laqueur holds that the new ways of conceptualising the body were actually new ways of

describing and constituting social life (Laqueur, 1987: 4). The new biology, which was primarily concerned with a search for fundamental differences between the sexes and an obsessive questioning of female sexual pleasure, developed at a time when the foundations of the old social order were being dismantled. Reconceptualising biological and social sex became a critical issue for theorising and organising the new social order.

In *The Woman in the Body* Martin focuses on the cultural meanings which are attached to the body. She argues that metaphorical language and images which are chosen to describe bodies and bodily events have profound implications for the way those bodies and events are conceptualised. This is borne out in statistics on events such as the rates of caesarean sections, and in women's impressions of medical accounts of their bodies and in their own bodily experiences (Martin, 1987: 14). Martin describes events such as menstruation and menopause and places them in a continuum in which representations of female biology and reproductive agency vary historically yet are consistent in that they are repeatedly depicted as being inferior to male biology and male agency. While this work helps create the space required to read social meanings into the body, Martin's earlier work is less interested in discussing the co-production of biology and social meaning, that is, the way they are necessarily contingent upon and specifically enjoin and constrain their mutual development, than it is in arguing for a looser synergistic relation between the two.

For my purposes, Laqueur and Martin's earlier work does not engage sufficiently with the production of meaning and material phenomena. This shortcoming mirrors a problem with Foucaults' work, namely a tendency to describe the body as a 'docile body' upon which cultural and social values are inscribed, rather than

attributing agency to the embodied subject (McNay, 38-43). However, by demonstrating the temporal and cultural malleability of the body each of these authors provide a means of teasing open the seemingly impenetrably enterprise that is the contemporary scientific construction of the body.

Randomised controlled trials and the scientific method

On the surface there are significant theoretical and methodological differences between the classic understanding of a 'scientific experiment' and the RCT as described in its ideal form. The RCT is an experimental method for determining the efficacy of competing therapeutic regimes through comparing two or more groups of subjects while they undergo treatment with different therapies. Subjects are allocated randomly to discrete treatment groups in order to minimise patient or clinician bias or selection effects which might influence the outcome of the trial. Observed outcomes undergo statistical analysis in order to determine whether any differences between treatment groups are statistically significant and should therefore be considered 'real'. If treatment outcomes are deemed to be statistically valid then judgements are made regarding the causal relations through which they were brought about and how these can be used to improve treatment options.

The purpose of RCTs is to create scientific confidence within the context of clinical practice. This means that the knowledge produced by RCTs is intended to be robust enough to be applied in clinics and health systems that are not identical, and to be generalisable to patients whose health needs and prognosis may vary from those of the trial participants. In other words, RCTs are supposed to reveal truths about real biological bodies. Because of the recognition that disease states and individual responses to them cannot be mapped precisely, RCTs do not attempt to speak in terms of definitive personal outcomes. Instead they emphasise

the statistical likelihood of outcomes within defined populations, and the generalisability of the outcomes to larger populations. In this context experimental 'replication' is not about direct and precise duplication of biological events between two or more individuals. Despite the continued desire within medicine to codify the operation of a universalised human biology, such a complete replication would be impossible given the myriad differences between individual life experiences.[1] Rather, researchers try to construct a version of replication within any given trial through testing a treatment in a number of individuals simultaneously and then attempting to minimise the effect of personal differences by averaging them statistically across the trial population when analysing results. By doing clinical trials researchers hope to achieve outcomes that are *generally* (with varying degrees of statistical likelihood) descriptive of the risks and benefits to the broader population. As well as repeating the general actions of a drug or procedure within a trial, replication also occurs at the level of whole trials, where researchers seek to implement treatments used by other trialists to ascertain the validity of experimental outcomes. This may be done through using identical treatment regimes or by adopting similar though slightly modified techniques. Provided no discrepancies arise between the outcome of the original and subsequent studies, this more fluid interpretation of replication is accepted. In the instance of controversy, however, such procedural distinctions become points of significant contention.

---

[1]Discourses about medical science are marked by a tension between descriptions about medicine as a craft skill wherein the experience and intuition of the practitioner is paramount, and the desire to standardise knowledge and practice. David Armstrong highlights this tension as it arose through post second world war clinical trials. As British researchers struggled to formulate methods for sound clinical research others highlighted the problems of applying science to medicine. L. Whitby, Regius Professor at Cambridge, said "it is true that medicine will never be an exact science because the normal variation in individuals have such a wide range that automatic and mechanical treatment is prohibited" (Whitby, cited in Armstrong, 1977: 600).

RCTs are, then, about generalisations within experimental populations rather than about the health of specific individuals. They often require very large numbers of patients in order to generate statistically significant outcomes and may also require large numbers of researchers. Consequently they may appear to be quite diffuse and cumbersome in comparison with traditional accounts of the strictly regimented scientific experiment. In practice however, the interpretive flexibility of the RCT is probably no different from that which is inherent in all scientific experiments. A more extensive account of RCTs follows in Chapter 2.

Sociology of RCTs

In the late 1980's Ann Oakley wrote that there had been very little sociological interest in the impact and methodologies of the RCT (Oakley, 1989: 27-28). With a few exceptions, the intervening years have not changed the situation despite the fact that the RCT, under the auspices of 'evidence based medicine' has continued its ascendancy (see for example Epstein, 1996; Richards, 1991). The tendency in medical sociology has been to address specific aspects associated with clinical medicine in ways which either ignore the science involved and focus on the human actions and institutional constraints, or else to look at instances and implications of erroneous science in clinical practice (Abraham, 1995). One reason for this may be that RCTs are a relatively new historical product, coming into use after the second world war and only gaining their professional appeal and the perception of their applicability to large populations during the last two or three decades. Consequently, the full implications of the institutionalisation of RCTs for policy and their impacts on the relations between and identities of clinicians and patients are still emerging. But another reason for the continued

paucity of critical engagement with the RCT may rest with the traditional immunity of scientific knowledge to social inquiry.

Although little sociological inquiry has engaged directly with the scientific content of medicine, critical analysis of many other aspects of the operation of medicine has paved the way for an examination of what counts as medical knowledge and how that knowledge is formulated. By demonstrating the systemic institutional and organisational prejudices operating in modern medicine, sociologists have made it more possible to question the self-evidence with which much medical knowledge has come to be regarded. Examples come from many areas; here consider the women's health movement. Feminist analysts have questioned the exercise of professional power by examining the way women experience health and the health care system as patients and as medical professionals. As I discussed previously, these critiques form an important part of feminist engagement with the question of science. Through investigation of specific instances, such as the policies and practices governing reproduction and fertility control, and by legitimising women's experiences as valid sites for analysis, feminists have been able to demonstrate ways in which social and political values are a constitutive part of medical practice and medical knowledge (see for example Ehrenreich & English, 1978; Holmes et al., 1980; Leeson & Gray, 1978). Questioning the representation of female anatomy and physiology and respecting women's experiences at the hands of doctors and clinical researchers reveals the systematic patriarchal subordination of women within medicine. Critiques of psychiatry and mental health, and the consumer health literature are other examples of sociological work which has destabilised medical knowledge (for feminist examples see Chesler, 1972; Chetwynd & Hartnett, 1977; for critiques of psychiatry and mental health see Goffman, 1961; Laing, 1976;

Rosenhan, 1973; Szasz, 1961; Szasz, 1970; Smith & David, 1975; for consumer health literature see Smith, 1991; Grace, 1994).

The theoretical moves which accompany a sociology of medical knowledge are similar to those which accompany a sociology of scientific knowledge and feminist critiques of science. Once it has been demonstrated that social and political values are embedded in the organisation and practice of medicine it becomes easier to argue that these values may 'get in' to the knowledge upon which medical practice is based. As with feminist empiricism, such a position is a shift away from a naive belief in the objectivity of medical science, and is often used to argue for a better or more robust exercise of the methods of science in medicine. Sociological literature on therapeutic evaluation frequently calls for an improved empiricism. While there are problems with arguing for 'better' medical science, as debates about feminist empiricism show, the call for improved research practice is a useful strategy for those wishing to challenge orthodoxy as it maintains the authority of medical science and can therefore utilise some of medicine's cultural resources while still pointing out contradictions in the status quo.

In 'Clinical Sense and Clinical Science', David Armstrong discusses the RCT from the perspective of the standard view of science. He sees the RCT as a method for improving the robustness of medical knowledge and making medicine more accountable to those outside the profession. His article can be read as representative of those who see problems with the operation and implementation of medicine but believe that increasing its scientific rigour will help resolve these problems and will make medicine more open, democratic and socially equitable. Armstrong describes clinical experience and knowledge generated by clinical

trials as the two sources of legitimacy for the medical practitioner. The two types of authority generated by these sources are not necessarily compatible and as the prestige of clinical trials has increased, scientific knowledge has become more influential in the clinic (Armstrong, 1977: 600).

This shift has caused a change in the behaviour of individual doctors and patients which Armstrong believes opens up the closed shop of medicine and creates a more equitable distribution of power in the doctor-patient relationship. He nominates three substantial ways in which 'science' has successfully disrupted the personal and professional dominance of medicine by elite groups of practitioners and made it more answerable to social scrutiny. First, the rise of scientific medicine has fostered a challenge to the traditional notion that 'clinical sense' rested in the personal experience of clinicians which in turn validated professional seniority and autonomy within the profession:

> Whereas different individual experiences of a problem could not be used to assert the correctness of one particular view, the total range of experience could be. Thus deference was paid to the clinician, usually the most senior, who had the greatest experience (Armstrong, 1977: 600).

In contrast, Armstrong believes that clinical trials offer the opportunity for the integration of the experience of a number of clinicians and create space for junior doctors to operate on a more equal footing with their senior colleagues. Secondly, the emphasis on the clinician's experience establishes a hegemonic relationship between doctors and patients so that a patient's individual experience of their condition is always out-weighed by that of their doctor. According to Armstrong, published literature from clinical trials now allows patients to gain access to information about their conditions which is not dependent on their doctor and

enables them to question their doctor's opinions. Finally, by emphasising a knowledge system based on personal experience, medicine removes itself from external scrutiny. Prior to the rise of the clinical trial it was difficult to assess the quality of medical care as observers could rarely claim the necessary experience to evaluate whether an outcome was the result of a treatment or of the normal course of the illness. Clinical trials allow treatment results to become public knowledge and thereby potentially contested by parties both within and outside the profession. Armstrong states that "knowledge in a system dominated by scientific method is no longer personal but universal" (Armstrong, 1977: 600). The consequence of the clinical trial is, then, a more open and democratic medicine where younger practitioners need not be hampered by the conservative tendencies of their senior colleagues, where patients are more equal participants in decision making, and where internal and external scrutiny of the processes of medicine thrive.

Armstrong is clearly arguing for the progressive powers of science in effecting beneficial social change. Unfortunately he does not support his analysis by linking it to the material practices of medicine, choosing instead to frame his work with an idealised account of science and the scientific method. If he had made this link it would have become apparent that 'science' is never self-evidently true but is always tied to a social and historical context. For example, what use are published trial results if patients are too sick to access them or their presentation limits lay understanding? And what use is an increased equity between junior and senior researchers if other obstacles limit entry to the profession in the first place? If scientific truth is understood as socially contingent, then its liberatory power is limited and perhaps ultimately rhetorical in nature. If science has a liberatory power it is as a result of a complex web of historical material conditions and the

social context that web produces. Contrary to Armstrong's vision, clinical trials are not sufficient of themselves to bring about beneficial social change. Although Armstrong praises the clinical trial as a tool to facilitate positive health reforms, he is praising a tool with limited investigative power. The various methods for conducting clinical trials cannot ask broader questions about the nature of medical science and the multiple ways it embodies and reifies the social relations which Armstrong hopes scientific medicine will eliminate.

Ann Oakley begins to address the social embeddedness of medical knowledge in *Who's Afraid of the RCT* when she struggles with reconciling science as a potentially progressive force with a feminist awareness of the limitations of western science and medicine. Unlike most other sociological writings about the evaluation of medicine, Oakley focuses specifically on the RCT. She discusses in detail the premise upon which RCTs are based and the methods through which they are put into operation. Her analysis maps ways in which feminist critiques of medicine stand to benefit from the RCT, as well as discussing areas of significant methodological concern. She identifies herself as a feminist sociologist who was responsible for designing and running an RCT in the area of prenatal health care. She is, therefore, situated within the feminist empiricist project. She tries to reconcile the RCT with critiques of science that include feminist concern with the social structure of science as being inherently sexist, racist, classist and a culturally coercive practice and form of knowledge (Oakley, 1989: 25). Citing the radical science movement, the emergence of ethnomethodology and feminist critiques about the masculine nature of scientific activity, Oakley stresses the "heightened awareness of the contribution made by different kinds of research strategies to extending human knowledge in the domain both of the 'natural' and

the 'social' sciences" (Oakley, 1989: 27). Knowledge is plural for Oakley, and an important part of that plurality is empirical science.

Oakley is responding in particular to feminist critiques of science and medicine as masculinized. She argues that feminist research is often identified with being on the 'qualitative' side of a divide in which 'qualitative' is seen as the preserve of the social sciences and 'quantitative' as being appropriate for the natural sciences. She assumes that the scientific method is beneficial, and she is interested in the dilemma of whether feminists can satisfactorily develop or appropriate that method without incorporating all of its oppressive masculine baggage. The specifics of Oakley's arguments warrant detailed consideration and are discussed further in the following chapter. Here, I merely identify her work as an example of a sociological attempt to understand RCTs. Her conclusions are that feminist appropriation of RCTs is possible and desirable. Provided that they are properly designed and adequately scrutinised, RCTs can contribute positively to the feminist health project. Further, she argues that they are a useful way of monitoring medicine's treatment of women. Women are under-represented in clinical research and their lives are over-medicalised by drugs and procedures which have not been properly assessed. RCTs provide a potentially beneficial standard through which this state of affairs can be addressed. But Oakley asserts that RCTs are not the only method available, nor are they always the best method. Feminists must remain mindful of the need to maintain a close scrutiny of the types of RCTs which are being used and the way they position female subjectivity. Oakley's commitment to the empirical sciences is evident in the article's concluding quote from Evelyn Fox Keller:

> The intellectual danger resides in viewing science as pure social product; science then dissolves into ideology and objectivity loses all intrinsic meaning. In the resulting cultural relativism, any emancipatory function of modern science is negated, and the arbitration of truth recedes into the political domain (Keller, 1982: 593) quoted in (Oakley, 1989: 53).

Oakley's article is a thoughtful attempt by someone bridging the disciplines of public health and feminist studies to de-stigmatise scientific medicine for a feminist audience. She rightly questions the feminist dichotomy between feminised and masculinized, qualitative and quantitative, and social and natural sciences. These dichotomies have come under increasing and sustained fire from other feminists who argue that they falsely reify categories which are actually more fluid and complex than the dichotomies suggest. One fear commonly expressed is that the material conditions of the natural world will cease to be given explanatory power and will be completely collapsed and redescribed as a product solely of social interactions. Such moves do not make sense within a public health that assumes and respects a division between the natural and social aspects of health. Oakley is seeking some way of incorporating anti-science critiques which question the very essence of modernism with the essentially modernist enterprises that are public health and medicine. She argues that one way to do this is to reclaim the methods of scientific medicine and address their shortcomings through the insights of feminist health. In so doing Oakley lays the foundation for a strong sociological critique of RCTs which engages with the organisation of scientific knowledge in more sophisticated ways than critiques such as Armstrong's. Oakley does not, however, move away from a dichotomous characterisation of social knowledge and scientific knowledge, nor does she take into account critiques which seek to do so or consider the consequences of such a move.

I want to extend the work of Armstrong and Oakley by developing an account of RCTs which takes a step towards dismantling the dichotomy between the natural and social sciences. Richards' work on the controversy over the efficacy of vitamin C for the treatment of colorectal cancer, brings a constructivist critique of scientific experiment to the genesis of medical knowledge (Richards, 1991). She examines the controversy which arose during the 1980s as Ewan Cameron and Linus Pauling sought to have their experimental results verified by the cancer establishment. During the 1970s and '80s Cameron and Pauling had consistently encouraging results from their use of mega-dose vitamin C as an adjuvant therapy for colorectal cancer. These results were not theoretically commensurate with the paradigm of orthodox cancer medicine, nor did they fit with the practices of orthodox cancer therapy. Richards provides a fine-grained historical account of Pauling and Cameron's efforts to have their treatment regime evaluated by orthodox means and she comes to the conclusion that the replication attempts came about not because of the epistemological merit of their theoretical position, nor because of the promising empirical results they produced. Instead, she argues, the cancer establishment was persuaded by the political and social authority Linus Pauling could mobilise because of his personal eminence and the resources which resulted from his alliance with the alternative health movement.

Richards describes the process whereby strategic allies are enrolled through convincing them that it is in their interests to support one's own work. Fact-making in science is a collaborative enterprise. In order to determine the validity of a knowledge claim and to protect it from criticism and dissent, it is necessary to enrol allies who participate in the construction and defence of the claim. This is not necessarily a conscious process and individuals may be drawn into fact-making negotiations when their own work is incorporated into the claims of others

(Richards, 1991: 174). Against all odds, Pauling and Cameron were successful in persuading the National Cancer Institute (NCI) to run an RCT of vitamin C for colorectal treatment. When the first trial contradicted Pauling and Cameron the matter was not simply closed. It is always possible for different interest groups to interpret results differently. Instead of conceding defeat Pauling was able to use his influential professional allegiances to negotiate another trial on the grounds that the first trial did not adequately replicate the work which upon which he and Cameron had based their findings. Scientific claims are constantly open to re-evaluation and re-negotiation, although the social and material costs are often great. It is the routine work of science both to carry out these constant negotiations and to obscure them from public view, and these negotiations always embody the values of competing interests.

Richards shows that the process of therapeutic evaluation is inherently social and political, and that the idea of neutral appraisal through the RCT is a myth. Arbitration over experimental findings is not a clean and predictable process, rather it is the result of behind the scenes negotiations which are often messy and unpredictable and cannot be codified within transferable scientific procedures. Further, they are always inextricably linked to the professional and wider social values and interests of those who are carrying out the evaluation (Richards, 1991: 174). Although such a strongly constructivist position is now increasingly common within the sociology of scientific knowledge, sociological critique of medical knowledge usually tends toward a more gentle constructivist position. Richards' work provides a model for my own in the way that it presents clinical medical knowledge as always and unavoidably the product of social interactions.

A shortcoming of Richards' work is its failure to engage with Oakley's concern that a strong constructivist critique of RCTs will collapse the natural into the social resulting in the replacement of scientific determinism with social determinism and an impotent relativism. Should such a collapse occur it would reduce the confidence of clinicians in their current decision-making practices, and rob patients of a supposedly neutral source of information against which to consider their experiences of their disease and their treatment. Although Richards provides a richly detailed account, she is primarily interested in analysing the disjunction between the rhetoric of experiment and justification in medicine and the practice of experiment, and the subsequent mechanisms of justification utilised in the vitamin C controversy. The need to improve and engage in clinical practice, themes present in both Armstrong and Oakley, appear to be outside the scope of her work.

One way of avoiding an apparent collapse of the natural into the social is to treat entities traditionally described as 'natural objects' as the condensed materialisation of historical and social meaning. Although these objects are thoroughly socially constituted, they exist and exert their presence within networks of meaning and upon other 'natural objects' in tangible ways. Examples of this approach can be seen among writers concerned with the problem of the body. Brian Turner, for instance, clearly insists on both the social and historical constructedness of the human body and the significance of the phenomenological subjective experience of embodiment (Turner, 1992). On one occasion Turner investigates 'the epistemology of the hand', considering the relationship between the physiology of the hand and its significance within our cultural system (Turner, 1992; chapter 3). Analytically dissecting the hand is a matter of interrogating its cultural and historical representation, and considering how they affect the lived experience and

potentiality of embodiment. But the hand is also an organism which, although made and remade in social discourse is constrained by biological possibilities and limitations. Turner asks whether "shaking hands, wavying hands, holding hands, binding hands, mutilating hands or cutting off hands" is of sociological significance. If so, what might be the embodied cultural consequences of human beings without thumbs (Turner, 1992, 100). The challenge for a sociology of clinical trials is to incorporate an awareness that medical practice, beliefs, and technologies are products of human actions, with rich, complex, contestable histories, with an appreciation of the frailty and coporeality of the entity on which they are enacted (the human body).

The structure of the thesis

The aim of this thesis is to develop an account of the ways in which medical knowledge and practice are used to naturalise socially and historically specific characterisations of gender identity. This is important because biological differences between the sexes continue to be used as grounds for limiting women's participation in society. Highlighting how various forms of biological determinism are used to justify patriarchal social relations is not a new project, but it is one which requires continuing attention given that arguments based in the natural sciences (which proponents of biological determinism employ) retain a special type of cultural authority which advantages them over arguments based explicitly in social knowledges. The proliferation of feminist scholarship and various critiques of modernism ensure that explaining differences in sexual identity as based solely on biology is no longer seen as a straightforward project. There is increasing appreciation within the social sciences and among health researchers and service providers of the extent to which biological identity and

personal well being are affected by psychological and social experiences. New areas of research continue to reinforce a sex/gender divide and to do so in ways which assume the biological and cognitive inferiority of women.

Equipped with the tools outlined in this chapter, I now turn my attention to developing a contemporary social history of justification in medicine. Chapter 2 begins this process by summarising and providing a historical overview of one of the key elements in the stabilisation of medical knowledge and practice, the RCT. From there, the thesis progresses by focusing on specific case studies to demonstrate how medical science is socially contingent local knowledge which embodies and perpetuates patriarchal assumptions about sex.

Chapter 3 describes the emergence of sex hormones as biological entities and examines the meanings which were and are attributed to them. It asks several questions: How have they been historically constituted and by whom? How has this constitution shaped current beliefs about hormones? Do sex hormones mean different things for men and women? And what role do they play in debates about biological and social identity?

Chapters 4 and 5 bring the preceding sections together by discussing how a particular hormonal drug - tamoxifen - is being tested in a particular set of RCTs. Chapter 4 outlines the current tamoxifen breast cancer prevention trials and examines how hormonal discourses and the discourses of science have been used by breast cancer specialists to persuade regulatory authorities and funding bodies that these trials are a safe and scientifically rational option. Despite the best efforts of their proponents, the tamoxifen trials have proven to be a highly controversial enterprise. Chapter 5 canvasses the debates, paying particular attention to the mechanisms by which controversies have been identified and the professional

identities of those responsible for dissent. How is the trial controversial and to whom? In what forums are these disputes being raised? Who is socially empowered to speak about the trial and why? And what does this mean for the social analyst of medical science and gender?

In Chapters 6 and 7 I turn my attention to the way medical science constructs male bodies and masculinity. The point of these chapters is not to develop an in depth account of the constitution of discourses about male sex hormones, but rather to draw out the differences between the medical construction of embodied women and the medical construction of embodied men. This is done explicitly from my perspective as a feminist researcher. To this end Chapter 6 examines discourses about men and hormones and locates them in debates about the role of sex hormones in prostate cancer, and Chapter 7 discusses some of the ways in which men and women differ as hormonally constituted cancer patients.

In conclusion I draw out the implications of the social history of RCTs and their role in the social constructions of sex hormones. Such a history can challenge perceived truths about biological sex and provide strategies for reform within the practices of experimental medicine.

CHAPTER 2

The RCT in medicine

RCTs are an historically located technological system comprised of physical artefacts (such as drugs), human activity (such as enrolling patients), and knowledge (such as the theory of randomisation) (see Law & Bijker, 1992)). This chapter describes the significance of RCTs within medical research. I discuss how ideas about science are represented within medical and sociological literature and by clinicians themselves as they write about their practice. The medical story about the RCT contains numerous internal inconsistencies, some of which are articulated, some of which are actively denied, and some of which are invisible to the clinical storyteller. I explore the factors which obscure these inconsistencies or prompt clinicians to live with them as they go about the business of building their social worlds. Further, I consider the process through which these inconsistencies are smoothed over and made to appear unproblematic or to disappear altogether. I also explore how the RCT constructs the clinician as a cognitively and socially disembodied knower and the experimental subject as the disembodied known and how different types of clinical trials change the ways these constructions occur.

The practice and theory governing the development and refining of medical knowledge and techniques changed dramatically during the twentieth century, and the theoretical and material practices which constitute the 'clinical trial' as we know it only came into alignment during the 1950s. This chapter begins by discussing representations of the RCT in contemporary historical accounts in order to explore the role of storytelling in science. There are numerous experimental methods at the disposal of clinical researchers and choice of research strategy is

contingent on factors such as the condition to be examined, the hypothesis in question, the experimental treatment, and the resources at the disposal of investigators. In the condensed accounts in medical textbooks these issues are represented in a way that glosses over the complexities of doing research while representing the RCT as the inevitable result of sound science in medicine and as naturally superior to other experimental methods. Textbook histories are contrasted with more rigorous historical accounts which tease out the question of how the RCT has become privileged without assuming it is the result of the method's inherent superiority. The second half of the chapter discusses different types of medical experimentation in order to draw out what makes the RCT unique and analyse how it is constructed in relation to alternative forms of medical investigation. The chapter concludes by focusing on the conflicting meanings of the RCT for women.

History of randomised trials

As well as making claims about the facts of a matter, the way that histories represent the world tells much about the historian and the social and intellectual order with which they engage. History is part of the way we give meaning to our world: as our historical accounts are made and remade so our understanding of and relation to the world change (Law, 1996: 52). The RCT, like all technologies, is a product with multiple histories.

As discussed in Chapter 1, a feature of the process through which science and medicine come to be seen as representative of the natural world is the way they obscure their links with social influences. This ability to obscure can also be present in the history of science. Historical accounts of science and medicine which try to pinpoint 'moments of origin' and 'discovery' in individual genius or

which present the development of knowledge and techniques as a smooth seamless evolution draw a picture of the world in which 'the truth' is always somewhere waiting to be revealed and articulated for us. To depict the history of the RCT in such a way is to attempt to naturalise it by illustrating both the length of the tradition of controlled trials, and the way this tradition has been refined and made more scientific throughout the centuries. The histories in medical textbooks and journals echo the Enlightenment commitment to the emancipatory power of the human intellect and contribute towards the hagiographical accounts of 'great men' and 'great moments' which are a rich tradition within the history and teaching of medicine (see for example Bailar, 1983; Bull, 1959).

Because of their pedagogical significance and their function in obscuring the social and historical development of clinical trials these accounts warrant consideration. A typical introduction to the history of RCTs, drawn from an orthodox epidemiology textbook reads: "Non randomised trials date back many years. L'Estang considers that the story of Daniel contained a report of a clinical trial" (Bulpitt, 1983: 5). The biblical book of Daniel contains the story in which King Nebuchadnezzar organised a 'trial', giving youths of royal blood a strict diet of meat and wine for three years. Daniel intervened and convinced the King to allow a subgroup of youths to eat pulses and legumes:

> Prove thy servants, I beseech thee, ten days; and let them give us pulses to eat, and water to drink. Then let our countenances be looked upon before thee, and the countenance of the children that eat of the portion of the King's meat: and as thou seest, deal with thy servants. So he consented to them in this matter, and proved them ten days. And at the end of ten days their

> countenances appeared fairer and fatter in flesh than all the children which did eat the portion of the king's meat (Daniel, 1: 12-17).

This story is widely cited (see Bull, 1959; Bulpitt, 1983; Feinstein, 1985: 684, to name a few; Meinert, 1986). Its admirers claim that it describes the rudimentary components of the clinical trial. They suggest that there are clearly identifiable control and experiment groups, and a defined intervention. Yet choosing to represent the genesis of scientific medicine in this way raises the question as to why the roots of clinical research can or should be located within a biblical story. The extract cited above does little to account for the precise nature or formation of the controlled trial, referring instead to a sacred text whose authority lies not in a factual history but with a faith in a religious tradition based on a miraculous God. Is the point of locating the birth of the RCT in this ancient text to demonstrate its enduring presence, its mythical significance, or possibly even its divine origin? One would assume that in accordance with the principles which govern science it must surely be the first of these, for mythology and divinity have no place within the rhetoric of modern medicine. Yet by using a religious text these narratives appeal to the discourses of miracles and divine intervention which are an important feature of the rhetoric of hope in medicine. As modern society emerges these histories describe how the divine magic in the old testament controlled trial has been replaced by the magic of science. In this way the two great cosmic powers, God and Science, are linked in the controlled trial, and it is through Science that God is laid to rest in modern medicine.

James Lind's experiments with treatments for sailors with scurvy is another historical highlight which is widely reported (Bulpitt, 1983; Feinstein, 1985; Meinert, 1986). Green states that Lind's experiment was the first documented

example of a therapeutic experiment with matched controls (Green, 1954 1087). In 1747 whilst at sea on board the *Salisbury*, Lind carried out a study in which he gave twelve sailors suffering from scurvy one of the following six different dietary regimes, these being cider, elixir vitriol and acidic gargle, vinegar, sea water, nutmeg, and oranges and lemons:

> On the 20th of May 1747, I took twelve patients in the scurvy, on board the Salisbury at sea. Their cases were as similar as I could have them.... The consequence was, that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them, being at the end of six days fit for duty (cited in Meinert, 1986: 5).

Although Lind's experiment indicated that oranges and lemons were the best treatment available for scurvy, the finding contradicted his own expectations. Consequently this example has an interesting twist which highlights the convoluted relationship between experimental outcomes, scientific knowledge and clinical practice. He was reluctant to believe that citrus was the most effective form of therapy, believing instead in the benefits of placing scurvy stricken patients in 'pure dry air'. Orthodox opinion at the time held that the way people experienced disease reflected an imbalance in an individual's 'humours', bodily forces which were as much spiritual and moral in origin as they were biological. To begin with there existed no belief system which could account for the apparent effect of fresh fruit on scurvy and there was also little reason for Lind to credit his experimental observations as it was not until after the re-constitution of disease as a specific entity in itself (which occurred in the mid nineteenth century) that the idea of comparative trials gained any theoretical importance (Meldrum, 1994: 12).

Despite Lind's findings, it took another 50 years for the British navy to supply lemons to its ships at sea (Meinert, 1986). At the time of Lind's original observations Britain was involved in the Seven Year War with France. Reflecting the assumption that clinical evidence speaks for itself, Green comments that it is 'strange' that the significance of Lind's results was not immediately realised (Green, 1954). If, however, one considers that his findings were at the time effectively 'irrational', that is, without rational theoretical basis, and if one considers that the provision of oranges and lemons to sailors would have been an expensive enterprise given that they were a culinary delicacy, prone to spoil, and used up valuable storage space, the reasons for ignoring Lind's anomalous observations appear more sensible. By the close of the century France was in the throes of revolution and the two countries were again engaging in war. The repeated hostilities with France increased the importance of maintaining a healthy fighting force which eventually resulted in the British testing out the provision of citrus fruit. But considering Lind's work through an essentially historical, political and economic lens does not make sense to Green whose concept of justification lies solely with the evidence provided by the clinical trial. Therefore he remains perplexed by the interval which elapsed between Lind's work and official recognition of his findings.

The conditions for and success of Lind's experiment were inextricably linked with the quest for British colonial and military power, adding another layer of meaning to the history of the clinical trial. Consider the following statement by Green made during a speech to the Royal College of Physicians of London in 1954:

> If, as seems probable, James Lind's account of his test of oranges and lemons against scurvy in 1747 is the earliest published description of a clinical trial

with carefully matched controls, it can fairly be claimed that the modern type of controlled clinical trial was a British 'invention'; it can be claimed with no less justice that this kind of trial in the form in which it has been developed since the end of the second world war is a very characteristic and respectable British institution, attributable in part, perhaps, to our native scepticism and our reluctance to take at their face value the over enthusiastic press reports that are too often published about new remedies when they are first announced (Green, 1954: 1085).

The status of this comment is unclear within the context of Green's speech. It certainly strikes this reader as humorous and may have been made to entertain his audience. However, as a moment of narration it works only through reference to existing social and historical discourses. It would seem that the clinical trial is not only historically indebted to British military might and colonial imperialism, but is also dependent on the natural scepticism which is at the heart of the rational British character. So far, then, this mythical history of clinical trials has woven together Christianity, militarism and nationalism to produce the fabric of scientific rationalism in medicine.

The next common turn taken in these hagiographic histories is to recount the medical advances made during the Second World War. Nationalism and the role of the military again feature in stories about the testing of penicillin, sulfa drugs, and the trials of streptomycin for the treatment of tuberculosis which occurred shortly after the war. According to Feinstein "[t]he evaluation of treatment for tuberculosis set the stage for the entrance of the modern era of randomised trials" (Feinstein, 1985: 687). When streptomycin became available shortly after World War II both clinicians and pharmaceutical manufacturers wanted prompt evaluation to justify

its use and production. Multi-centre trials were undertaken in the United States in 1946, although the trials did not use any form of control group. The supply of streptomycin in the UK was limited, which prompted British researchers to include control groups within their trial design. Their study was confined to a subgroup of severely ill tuberculosis patients. Green writes:

> The shortage of streptomycin in Britain at the time (which was so distressing from the humanitarian point of view) here proved scientifically advantageous, for it allowed the Committee [governing the trial] to arrange, with a clear conscience, a rigidly controlled trial of the value of bed rest with streptomycin, as compared with bed rest alone, in young adults with rapidly advancing bilateral pulmonary tuberculosis… (Green, 1954: 1089).

Green identifies the key features of the investigation as being the random allocation of patients to either control or experimental group and the blinding of radiographers to the treatment each patient was receiving (Green, 1954: 1089).

Initially the British researchers saw the use of a control group as ethically acceptable only because of the shortage of streptomycin. The contingencies of the material availability of the drug during the immediate post-war reconstruction determined this aspect of the design of the trial (Green, 1954: 1089). The 'scientific benefits' of using controls would probably have been bypassed had the material conditions been more favourable as they were in the US streptomycin trials. Conflict between ethical and scientific priorities is a regular feature of debates about clinical trials, and so too is the flexible deployment during a controversy (and the posthumous reconstruction after its conclusion) of what counts as being 'ethically appropriate'. Further, by being required to select a specific subgroup from a patient population with a disease with a widely variable natural history

investigators were able to choose relatively homogeneous groups with similar clinical presentations. 'Natural history' of a disease refers to the course of a disease from onset to resolution (Last, 1988). The use of the term reinforces medicine's assumption that disease is a 'natural' entity rather than a socially and historically variable phenomenon. By tightly controlling the selection of patients researchers managed to avoid the problems (such as the different effects of a drug on people of different sex, age and stage of disease) which would emerge later when randomised trials were used in more heterogeneous groups of patients with the same disease. Finally, because of the limited availability of streptomycin, and the visible and immediate improvements which patients experienced, the trial had a short duration, so the long-term adverse effects of the drug did not surface until later (Feinstein, 1985: 687-88).

The historical episodes recounted here, and more importantly their historiographical treatment of events and people, involve storylines and subjects which are archetypical within the history of science. They assume explanations which are similar to those used by science. Along with populist myths about the benefits of science, these are histories which tell of intellectual emancipation, where individual initiative overcomes the limitations of circumstances and the protagonists take on heroic status. Although the incident recounted are discrete events they are connected in structure and rhetorical meaning by this myth of the beneficence of science thereby forming a cohesive narrative when placed together. Each occurrence is described as a significant advance on the preceding state of affairs (Olby et al., 1990: 8).

In contrast, Harry Marks' history of the Collaborative Clinical Group (CCG) is full of antiheroes and government conspiracies, problematising the ideal of the

seamless progression towards increasingly scientific medicine. Marks is an advocate of RCTs, stating that contemporary clinical trials featuring randomisation of patients and blinded assessment of outcomes "represents an unparalleled technique for measuring the value of novel treatments" (Marks, 1988: 297). However the RCT which Marks supports is fundamentally different from the one upheld by authors such as Green, Bailar and Meinert. The point of Marks' argument is to demonstrate that, rather than being the result of conceptual breakthroughs and individual innovation, controlled clinical trials emerged as a research form only when bureaucratic, financial and clinical interests had been aligned in such a way as to provide the social conditions in which that form of study could take place. This alignment was brought about by the active work of researchers and government agencies and was opposed and subverted by clinicians and pharmaceutical companies (Marks, 1988; Marks, 1997).

According to Marks, examples can be found of medical researchers who were attempting to carry out 'modern' clinical trials prior to the streptomycin trial for tuberculosis in 1948. Marks details several clinical investigations, including the Cooperative Clinical Group's (CCG) experiments with syphilis treatments (1928-1935), and the studies of tuberculosis by the Veterans Administration (VA) in the USA, and Public Health Service (PHS) in the UK, following World War II (Marks, 1997: chapters 2 and 4). He argues that their design and execution contained key elements of modern clinical research methodology. Although these investigations did not produce coherent and definitive findings, this was not the result of shortcomings in the research design. Instead Marks proposes that these failures were in large part due to the dominant culture of medical research and the way individual clinicians and social institutions operated within that culture (Marks, 1988: 298). In other words, although unsuccessful in achieving their articulated

goal, the syphilis and tuberculosis trials are a part of the networks of agency which contributed towards the reorganisation of the culture and practice of medical research away from one which emphasised individual expertise, towards one which stressed a norm of shared professional knowledge.

The feature which identifies the CCG, VA and PHS studies as intellectually interesting and distinct from other contemporary research was their attempt to organise clinicians into a culture of communal research. As discussed in Chapter 1, prior to the rise of clinical trials individual experience and expertise was the only standard considered appropriate for judging therapeutic success, and there was no particular place for, or virtue associated with, ideas about joint investigation. The initial appeal of cooperative studies lay in the belief they could help overcome the limitations of individual research by studying large numbers of patients in order to offset the effects of spontaneous recoveries, and by joining together a number of experienced clinicians to consider a specific problem, thereby reducing the effects of individual clinician bias. It was also hoped that they could produce a standardised way of selecting patients, providing treatment and analysing results in a research setting (Marks, 1988; Marks, 1997).

The Cooperative Clinical Group

In March 1928, Professor John Stokes of the University of Pennsylvania invited a number of high profile researchers to join him in forming the Cooperative Clinical Group (CCG), and in conducting a multi-clinic evaluation of the treatment of syphilis. At the time there was no consensus on syphilis treatment. A range of drugs was commonly being given in varying strengths for a condition whose presentation, prognosis and natural history were ill defined, all of which made evaluating competing treatments a difficult task. The CCG felt that general

practitioners should look to the specialists for guidance on the best methods of treatment (Marks, 1988: 301). They believed that, as leading specialists in the field of syphilis medicine, their combined experience would be of more value than the individual experience of general practitioners or the research efforts sponsored by pharmaceutical companies. As a collective research enterprise, their mandate was to develop an authoritative base from which to assess and subsequently recommend treatment regimes; however, finding ways of generating consensus and cohesion within this group proved a difficult task.

Standards literally had to be developed from scratch. Amongst other considerations the group had to agree on a model for the 'normal development' of syphilis and then decide on which stage of the disease to investigate. They needed to document the range of existing treatments, decide which should be studied, and in what order. They had to generate criteria for inclusion or exclusion from the trial, agree upon indicators against which success or failure could be measured, and decide who should carry out the assessment (Marks, 1988: 301). These questions are a part of any modern clinical trial, however researchers now have cultural and material resources on which to draw, including historical precedents, standardised methods, manuals of procedure, and other researchers trained to follow the requirements of centralised trial organisers. Even so, agreement over the design and operation of trials can still be fragile when parties seek to consolidate their research interests. The CCG was attempting to work in a novel way. To generate solutions to these problems they needed to arrive at a genuine consensus among a disparate group of people whose professional integrity rested largely on their ability to act individually and in accordance with their own experience. To be successful they needed to reach a consensus which was binding among researchers who had no prior experience of, or commitment to, joint research. In the end the

task proved too difficult, as differences of opinion persisted and consensus remained elusive (Marks, 1997: 53-59).

For an example of the difficulties facing the group, consider the problem of which stage of disease and what treatment regimes they should study first. To begin with, interpreting symptoms proved to be idiosyncratic and individual doctors' accounts of clinical presentation often varied from patient to patient and contradicted their colleagues. Patterns of clinic attendance and record-keeping also differed between clinics, and treatment history was generally poorly documented which compounded the problem of assessing and standardising treatments. It was often difficult to work out what treatments patients had received, the stage of their disease at presentation, whether they had recovered regardless of treatment, whether they relapsed despite treatment, or whether they had been infected anew. Further entanglements were experienced when senior investigators delegated the classification and coding of patients to statistical staff who lacked clinical experience. Publicising the results of the CCG's work proved another stumbling block, as summarising and outlining their findings had generated much contention within the group. According to Marks:

> Stokes and Moore, the two members who had worked most with the data, were especially cognisant that behind each 'fact' lay a series of decisions, often controversial, and sometimes inconsistent, concerning the classification and interpretation of the data (Marks, 1988: 304).

When the group was eventually able to overcome its internal conflict and publish, their findings did not make much impact on the medical establishment in the short term, although subsequently they have been considered as landmark research.

Marks attributes the failure of the CCG to a shortage of financial and personal resources which was not simply material, but cultural as well. The major barrier to the CCG's success was the difficulty of getting participating research physicians to forgo their intellectual autonomy and to treat patients in accordance with the requirements of the trial:

> As chiefs of prestigious clinics, the members were good at giving orders, and as former interns they were good at taking orders, but neither experience equipped them to share authority. They excelled at originating novel ideas and at criticising other people's work, but not at jointly resolving differences of opinion (Marks, 1988: 308-9).

The Group lacked financial support, equipment and drugs, but the problems the principal investigators had in relinquishing control of clinical practice and data analysis were equally crippling and made complicated issues, such as measuring the severity of disease or the treatment outcomes, all but impossible to resolve (Marks, 1997: 57). Despite all these dilemmas, the work of the CCG eventually gained a degree of recognition and became a standard against which other investigations could be judged.

The conditions under which the CCG worked changed dramatically with the advent of World War II. In both the UK and the USA the war increased government interest in both the funding and the organisation of medical research. In USA monitoring of medical research was centralised in the Committee on Medical Research (CMR) through the Office of Scientific Research and Development. The increased role of government and military during the war fostered elite medical researchers and their interest in cooperative research. Leading specialists could be seconded to work on specific well-defined problems

with the directive that it was in the national interest to find the most efficient solutions (Marks, 1988: 309).

Due to shortages during the war the CMR was made responsible for rationing experimental drugs. When, in 1943, it was suggested that penicillin was effective in treating syphilis (a major health problem within the armed forces) a trial was organised at the request of the Army with Joseph Earle Moore, a former member of the CCG, as chief investigator (Marks, 1997: 108-13). Because the military medical bureaucracy could control clinical access to a scarce and highly sought-after drug, the trial organisers were able to extract agreements from participating clinicians to abide by the treatments outlined in the trial design. Initially Moore and his team were successful in recruiting both participating clinics and patients; however as penicillin became more readily available clinicians increasingly broke the trial protocol. Compliance, it seemed, rested not solely on their commitment to the research ideals and methodology but required a degree of coercion by state regulatory bodies, demonstrating again the unwillingness of physicians to relinquish their individual clinical autonomy to external forces. Failure to stick to the protocol and poor follow-up meant that nearly half of the patients enrolled in the syphilis trials during the war could not be counted in the final results (Marks, 1988: 310).

The recurring problem of clinicians' desire to maintain control of the treatment of their patients during clinical trials was tempered somewhat by the introduction of randomisation into trial design. Although clinicians were becoming increasingly sympathetic to the concept of cooperative trials as a good way to carry out research, in practise it had proven difficult to maintain their commitment. The model of centrally controlled randomisation adopted by the British Public Health

Service's trial of streptomycin among soldiers with tuberculosis was introduced on the grounds that it would reduce the need for subjective input from clinicians. Clinicians could be persuaded to relinquish their personal and professional responsibility for treatment as they were doing so in the faith that randomisation was a scientifically reliable process which should overcome the fallibility of individuals. A consequence of randomisation which was not widely publicised was that it would also reduce the ability of individual researchers to stray from an agreed research plan (Marks, 1988: 319-29).

Marks' account of the CCG highlights the work of organising people and things as a requisite for 'success' in scientific research. This work is not simply a matter of obtaining financial and institutional resources, but reaches to the heart of the research effort through the ways it shapes the identity of researchers and the knowledges and practices they produce. Marks argues that the CCG 'got it right' intellectually by trying to generate a culture of cooperative research. This collaborative approach amounted to a major advance in clinical research but could not be understood as scientifically beneficial until the work of making adjustments to the social conditions governing medical research had been carried out. These adjustments were facilitated by pressure from government and were actively resisted within the profession, yet they have subsequently been constituted as a self-evidently beneficial cultural reorganisation resulting in a methodologically more enlightened profession.

The identities of clinical researchers being constructed by histories like Marks' are quite different from the identities constructed in medicine's own hagiographies and Whig histories; and they are much less flattering. No longer are the clinical researchers heroes leading a hapless public on to a brighter future. Instead, they are

a disparate and self-interested group who need to be corralled into collective projects in which they have little faith and little interest. Participants in the CCG are described as unwilling and unable to reach consensus, easily distracted by their own interests, and unwilling to relinquish control of their clinical autonomy to a central organising body. As the recognised experts in the field of syphilis treatment, their behaviour and actions reflect the state of knowledge and treatment practice in the field. Knowledge about syphilis was fragmented, uncertain, and personally generated through the experience of individual clinicians who could not arrive at a consensus on what that knowledge might be. Experience amounted to individual intellectual property and could not be shared amongst the community of professionals despite the best intentions of individuals involved. Successful treatment depended on the clinical experience of the treating practitioner.

The advent of World War II saw a rationing of existing resources and an increased pressure to maintain fit and healthy armed forces. Money and drugs for research were more readily available but only to those who were prepared to follow the directions of a central organising committee. Clinical researchers became part of the war effort and part of a chain of command. They lost their professional autonomy, becoming instead agents working for the national good, and their knowledge and experience became part of the collective strategy to bring about victory. When individuals objected to this change in their identity, military and government pressure could be used to remind them of their obligations as citizens.

Marks constructs the RCT as an artefact which strips individual researchers of their autonomy and authority and tightens the centralisation of medical research in the hands of a few individuals who are in close relationship with government and corporate capital. But if this description of the historical evolution of clinical

researchers is challenging, consider for a moment his treatment of medical subjects. Patients are all but invisible in his account; they are the absent 'other' in the making of modern medicine and can only be read between the lines of the main story. To begin with, patients for the CCG were unrelated diverse clinical 'presentations', with a non-existent or uncertain history (in the form of medical records), and an unreliable sense of their own state of health. In order for scientific work to be deemed successful, these patients had to be organised into a relation with their disease and others suffering from that disease (through codification into discrete categories along the spectrum of a normal 'presentation'), and a relation with their doctor and their bodies (through a reinscription of personal history and self knowledge into a deference to clinical authority). The CCG were unable to bring about this reordering in patients' behaviour and although it is the failure of doctors to discipline themselves which is the focus of Marks' commentary, their inability to produce disciplined medical subjects also contributed to their failure. It is perhaps not surprising that the first RCT which was deemed to be successful involved soldiers and ex-soldiers as its medical subjects: as successful patients, this group embodied the rhetorical ideals of discipline and altruism.

Science, identity and contemporary medical research

The first half of the chapter has focused on different histories of clinical trials and the meanings they convey about science, medicine and medical research. The historical accounts medical researchers favour for themselves (those taken from textbooks and medical journals) have been contrasted with another history, and two narratives have emerged: one telling of the unproblematic evolution and natural superiority of the RCT, and the other describing its emergence as a result of slow and arduous (and at no point self-evident) work by researchers,

government and the military. The remainder of this chapter explores how concepts of medical rigour and science are taken up in descriptions of current research methodologies.

There are two principal types of study in clinical medicine: descriptive studies, such as correlational studies, cross-sectional surveys, and case reports and case series; and analytic studies, such as case-control and cohort studies, and intervention studies. Each of these forms of research appeals to and mobilises different features of the rhetoric and mythology of science. Before exploring how notions of rigour and science are taken up in medical literature these study methodologies are briefly described.

Descriptive Studies

Descriptive studies are primarily concerned with describing the general characteristics of a disease, particularly in relation to individuals and populations, geographical locations and historical time frames (Hennekens & Buring, 1987: 16). This 'trend mapping' is a valuable technique for formulating policy, developing education campaigns and allocating resources, and it can contribute towards identifying factors which may be responsible for causing the disease or conditions in question. Descriptive studies use information from a broad range of sources including census data, vital statistics records, employment health examinations, clinical records from hospitals or private practices, national survey data on consumption of foods, medications and other products (Hennekens & Buring, 1987: 101).

The three main forms of descriptive study are correlational studies, case reports and case series, and cross sectional surveys. Correlational studies identify

representative features within a population in order to describe disease in relation to some specific factor such as age, date and time of an event, exposure, or development of a condition, the use of health services, and so on. The primary advantage of a correlational study is that existing data sets are often available, making the research comparatively quick and inexpensive (Hearst & Hulley, 1988). Hennekens and Buring identify two chief limitations of the correlational study. Because they seek to describe rather than analyse health trends in specific populations, they are unable to link exposure to disease in any particular individual. Their power thus lies in the strength of observational inference they can lend to support an existing causal hypothesis, or in the possibility that their findings can contribute towards generating a causal hypothesis.

An example of this is the study by Schatzkin et al., which examines the correlation of patterns of alcohol consumption with the prevalence of breast cancer. By considering measures that represent alcohol consumption alongside measures that represent dietary fat intake and the occurrence of breast cancer, Schatzkin and colleagues found that there was no independent association between alcohol consumption and breast cancer (Schatzkin et al., 1989). As this study is descriptive only, it does not shed light on which of a number of different competing factors might be responsible for causing the breast cancer of any particular women or the cancers in any specific subgroups of women, or in the general population. Alternatively, should no theories exist about the causes of breast cancer Schatzkin's descriptive study would be a useful attempt to generate an initial causal hypothesis about the relationship between alcohol consumption, dietary fat intake and the incidence of breast cancer. As correlational studies do not attempt intervention, and often rely on pre-existing data, they lack the ability to control for the potential effect of confounding factors (influences which are not of interest to

the researcher but which nonetheless affect the data generated during a study). The existence and effects of such confounding factors may be hinted at by descriptive studies, but descriptive studies can not be considered scientifically conclusive.

A case report or case series documents the history of an individual or a small number of individuals. Case reports may simply summarise a patient's symptoms or the way these symptoms change over time as a means of identifying the 'normal' presentation and development of conditions; but more often they focus on cases which are considered to be unusual or anomalous. In terms of the standards of science, case reports and case studies are not considered to be reliable as they are purely anecdotal, although they do provide an important link between clinical practice and research because they allow practitioners to speculate directly as to the reasons for an anomalous presentation whilst supposedly alerting researchers to the existence of a deviation from the expected presentation of a disease or condition. Case reports are among the studies most frequently published in medical journals and have historical importance in epidemiology because of the role they play in identifying a potential epidemic (Hennekens & Buring, 1987: 106).

An extension of the case report is the case series in which a number of case reports dealing with what is assumed to be a single condition may be grouped together to document different examples of the condition, different interventions, and different outcomes attributable to these interventions. If a clinician is detailing the effects of different treatments in a small number of patients, the case series may provide a miniature model of an intervention trial. Merit in modern medical trials is always linked with the statistical power attributable to a trial population and the perceived objectivity of the researcher, so the numbers contained within a case series are

always too small to be considered meaningful. Instead, they are important for providing clinicians with an avenue through which to report on unique or unusual patients. The case study is not considered to be a scientific mode of knowledge production. As with correlational studies, case studies may be useful in formulating hypotheses, but are not appropriate for testing such hypotheses.

The final type of descriptive study is the cross-sectional or prevalence survey. Cross-sectional surveys provide details about the frequency of occurrence and nature of a disease by producing a 'snapshot' of the health status of the population at a specified time (Hennekens & Buring, 1987: 111). In these studies an exposure or risk event and disease status are measured among a group who are defined by a specific set of characteristics. A particular time frame or another identifiable event may be the reason people are chosen. As with other descriptive studies, cross-sectional or prevalence surveys are mapping techniques which are useful in measuring the health status and needs of a population and in developing and assessing policy. They are particularly useful in identifying the needs of specified sub-groups within a community and for suggesting intervention strategies for those populations. For example, they can be used to gather information on the prevalence of disease or health outcomes in certain occupations, thus indicating the need for reviews of workplace occupational health and safety management.

Although they are said to be 'descriptive', the types of study listed above all involve a degree of inferred analysis through the ways in which they order and document information and events. Inference is drawn about what is considered to be a base level or 'normal' state of affairs (as with a cross-sectional survey) or about the way a population's experiences or individual cases (as with case studies and case series) differ from an expected norm. Essentially, however, they claim to

observe and represent in an unbiased manner, the state of a population's health. Once this has been done, researchers can speculate on cause, but cannot test it with the methods of descriptive studies.

Descriptive studies are considered to be the least scientific of the methodologies available for medical investigation, and examining how they fashion researchers and the researched may shed some light on why this is so. Initially they represent researchers as being observers only. Although this is in keeping with traditional assumptions about scientists as observers of nature, it limits the primary identity of researcher to 'reporter' rather than 'innovator'. Through their reliance on existing source material the researcher conducting a correlational study, a cross-sectional or prevalence survey is made to be an expert data manager rather than an expert clinician, and indeed, they need not even be medically trained. These methodologies assume that medical practice results in vast data bases and that medical knowledge is best served by linking and aligning this information in specific ways so as to represent accurately the health of populations. With the exception of case studies and case series, the research subjects in descriptive studies are populations not individuals. They are situated populations: people with histories, dietary habits, work practices, health service utilisation patterns. They are populations who are routinely monitored and tracked by governments, employers, insurance companies, and hospital administrations. The human bodies in these studies are thoroughly embedded social subjects whose health is contingent on the way their activities are given meaning through surveillance techniques available to researchers. By drawing on material gathered from large surveys and existing health data bases, researchers utilising these methodologies are also constructing themselves as part of a system of social surveillance and

management - an identity which is at odds with the ideal of the good scientist and her/his object of study as existing outside the constraints of the social world.

The case report or a case series has a special and paradoxical place within the rhetoric surrounding clinical research and the identity it helps build for clinicians and patients is quite different from the identities created by other descriptive or analytic studies. Initially they speak of a direct personal relationship between patient and doctor. Here, the subject is not a population, but an individual. The patient is of interest solely because of their deviance from the clinical experience of the doctor. By nominating their patients as unusual, the clinician is assuming their personal clinical experience as an authority for judging norms of health and disease. They alone are endorsed to judge the clinical interest of a patient who is assumed to be an anomaly from a universalised norm (see Hunter, 1991, especially chapter 5). It is, however, this individualising emphasis on both the experience of the medical practitioner and the patient which reduces the scientific merit of the case study or case series. A scientific clinical researcher is one who remains detached from and disinterested in their patients, and a scientifically useful patient is one who can be made to fit within codifiable and generalisable organisational schemes and is not a problematic unique exception to the rules. Despite this, the personal experience of a doctor is still a respected platform for clinical decision making which may contribute to the high regard in which case studies and case series are held.

Analytic Studies

The second major class of medical studies are the analytic studies such as case-control and cohort studies and randomised controlled trials. Cohort studies involve following a group of people defined by a specific characteristic or set of

characteristics over time. They serve both a descriptive and an analytic purpose. They are descriptive inasmuch as they document the occurrence of a single or multiple outcome within a population, and then seek to analyse the association between hypothesised risk factors and those outcomes. Cohort studies can be both prospective (the samples, risks and outcomes of interest are identified prior to the events occurring) or retrospective (the events of interest or outcome have already taken place).

According to Hennekens and Buring case-control studies are more scientifically robust than cohort studies because they introduce a control group against which risk factors and outcomes among the cases are compared (Hennekens & Buring, 1987 133). Cohort and cross-sectional studies are described as 'lacking the strength' to investigate all but the most common diseases; they would be expensive and would require thousands of subjects to identify risk factors for less common diseases. By introducing a reference group, the power of a study is increased through allowing the prevalence of risk factors in those with a disease (cases) to be compared with the healthy reference group (controls). Cases and controls are analysed with respect to some existing or past event or exposure which is thought to be causally related to the disease or condition (Meinert, 1986: 283). Such analysis is generally retrospective but under certain circumstances can be prospective. This design is seen as being particularly susceptible to bias where the selection of cases and controls is concerned. For example the defining characteristics of both cases and controls are specifically chosen by the researcher. Consequently the researcher can manipulate directly (consciously or otherwise) the identity and definitions of who and what constitutes an appropriate research subject. This is thought to be problematic because of biomedicine's commitment to the neutrality and objectivity of researchers. Besides the potential for selection

bias, the long time spans which are sometimes involved with retrospective studies and the way exposure is recorded in both cases and controls is another point at which bias can occur. In particular, in the absence of adequate record keeping, personal recall is seen as unreliable. The temporal reversal of the causal chain, that is moving from effect (disease or health event of interest) to cause (antecedent exposure or event) has led to some scepticism amongst investigators who see it as less logically robust than moving from cause to effect (Hennekens & Buring, 1987 133). Despite this, Newman et al argue that when diseases are either rare, or have a long latent period between exposure and onset, case-control studies are far more efficient than the other designs, and "are often the only feasible option" (Newman et al., 1988: 80).

The perceived weaknesses of cohort and case-control studies undermines the scientific identity of a researcher in two ways. Initially, researchers may be held answerable for bias in the selections of participants (something against which the process of randomisation guards). Secondly, where the study is retrospective the researcher is cast in a passive role, merely recording the experiences of trial participants. Although the researchers design surveys and interview schedules the intellectual authority of the study is to a large degree dependent on the accounts participants give of their lives: it is not the researcher who interprets the physical signs and symptoms of study participants, but the participants themselves who interpret the surveys and interview schedules. And again, as with the descriptive studies, these are socially situated subjects whose life-histories are crucial in determining their eligibility for participation in a study.

Whatever their limitations, all these forms of medical investigation are widely used and are highly valued; the most important aspect of good clinical research is

rigour which includes assessing at the outset of a project which method of study is most suitable. Different problems require different solutions, and the way a problem is understood to operate goes a long way toward thinking about how solutions may be achieved. Several factors influence the choice of research methodology, including the condition, event or disease under investigation, and the time frame within which the research will take place. Also important are the personnel available to participate in the project both as researchers and subjects, the nature of the intervention under investigation and expected degree of participant compliance. Finally, funding considerations are crucial. The particular strengths and weaknesses of trial designs cater differently for the contingencies of specific problem solving exercises. The first task in approaching an investigation is to arrive at an appropriate methodological design. What precisely 'appropriate methodological design' might mean is constantly the subject of vigorous and critical debate within the medical research community. However moves towards 'evidence based medicine' (such as the Chocrane Collaboration) argue that RCTs are the most scientific method and suggest that in the best of all possible worlds they should be the method of choice.

In light of the acknowledged value of descriptive, case-control, and cohort studies, why has the RCT risen to such clear epistemological prominence, and why is knowledge derived from RCTs considered to be superior to knowledge derived from these other forms of experimentation? Why do researchers in one breath utter statements about the need for diverse research strategies and trial designs, yet in the next breath identify them as less authoritative than RCTs. For example, Mosteller et al write of the RCT:

Many other, simpler strategies also provide information about what happens after treatment is given. Each of these strategies is sometimes used to say something about the effectiveness of a treatment. They all lack the strength of the controlled trial because their designs are inherently weaker.... They are frequently described as being almost as good as or closely approaching, but never is it suggested that their weaker design offers the strength of inference one can provide with a controlled trial. For this reason, the carefully executed controlled trial continues to supply our best evidence of cause and effect. (Mosteller et al., 1983: 14).

And in the next paragraph:

> ... in the controlled trial we have a model of perfection...(Mosteller et al., 1983: 14).

The RCT

The term 'randomised controlled trial' is generic, referring to a set of intellectual and practical approaches to identifying the relative merits of specified medical interventions with the aim of generalising the findings to the clinical setting (Bailar, 1983 2). A trial is said to be 'controlled' when a researcher actively assigns a placebo, single or multiple competing therapies to one or more experimental groups within a larger population (Mosteller et al., 1983: 13).

In theory, a good trial has tightly defined criteria governing eligibility for participation. There will always be a 'control' treatment against which the experimental treatments are assessed. This control may be a placebo (considered to be inactive), or it may be an available standard treatment. There may be one experimental agent, a number of different agents or combination of agents, and the

number of control arms in the trial will vary according to the number of treatments being investigated. Allocation of patients to either the control or experimental groups is critical and, as indicated by the discussion in the preceding section, is seen as a point at which 'bias' can enter a trial. Consequently it is thought to be vital that this allocation be completely 'random' and beyond the influence of participating clinical researchers or the subjects themselves.

The addition of randomisation to trial design is seen as a major contribution to scientific medicine because it supposedly guards against selection bias. When randomisation is effective the allocation of treatment options occurs in a totally unpredictable manner, eliminating the possibility that clinicians' personal interests can affect the composition of the groups (Feinstein, 1989: 481). It cannot be overstated how significant this aspect of randomisation is thought to be. As well as addressing the problem of active selection bias, random allocation theoretically ensures that within the chance aberrations produced by the randomised 'luck of the draw', the groups receiving the different treatments should have similar prognostic outlooks before treatment begins. Ensuring adequate randomisation is essential for smoothing out and counteracting the differences that individual patients and physicians may bring to a trial situation. Thus randomisation is essential to the belief that a well executed trial will result in a conclusion that is generalisable and representative not just of the trial population, but of the population as a whole.

How randomisation actually happens will vary, depending on the individual trial design. It may involve sealed envelopes containing details of the arm of a trial to which a patient will be allocated, or a prepared chart listing the same information (Hill, 1951: 280). A table of random numbers may be used, or a computer program generating random lists (Hennekens & Buring, 1987: 186). It is important that

randomisation not be open to corruption, so it is considered desirable to have a centre of randomisation at a different physical location from the trial site. With many modern large-scale multi-centre trials the statistician in control of randomisation is located away from any of the clinical sites.

Blinding, the process whereby as many of the people as possible who are involved with the research are prevented from knowing which of the therapeutic agents each trial participant is being given, is the next significant feature of the RCT. Blinding is said to be important to maintaining neutrality and impartiality throughout the experimental process. Initially, if clinicians and researchers know which treatment patients are being given they may lose their natural professional objectivity and interpret observations and outcomes in a manner which favours their preferred outcomes. The more blinding, the better. Thus it is desirable to extend blinding to all those handling materials deriving from the trial (for example radiologists or pathologists). In the ideal situation the blinding extends well beyond this. It is also important that the trial participants are blinded for two reasons: firstly there is some hint that if patients know they are being given an experimental agent they may well actually do better simply because of that knowledge. Secondly, and more significant for the requirements of RCTs, if patients know which agent they are being exposed to and if it is not their agent of choice, then they may withdraw from the trial and seek alternative treatment, or corrupt the trial by seeking additional treatment 'on the side'. Any of these would undermine the research on three fronts. Every withdrawal must be considered when calculating the results and may require the withdrawal of another subject from the opposing arm of the trial which can weaken the statistical power attributable to outcomes. Seeking additional treatments may affect the actions of experimental therapies and confound outcomes in ways which researchers cannot account for. Finally, when

participants withdraw from a trial or seek additional treatment they challenge the research clinician's authority to determine what constitutes best treatment (even when blinded themselves to what the treatment might be).

As suggested in Chapter 1 and in the preceding discussion of the history of clinical trials, blinding presents a paradox in the operation and ideology of medicine. It serves to maintain and further reify the scientific (as opposed to clinical) authority of researchers while assuming and formalising a fundamental lack of authority or expertise among trial participants. By attempting to maintain the neutrality and disinterestedness of the clinician, blinding seeks to reinforce their cognitive and professional authority. Appeals to a professional neutrality and disinterestedness are a fundamental part of the claims upon which medicine maintains its privileged social status. Blinding within professional groups therefore lends support to this claim. Blinding within patient groups, on the other hand, is directed at stopping patients making decisions about treatment during a trial and in so doing threatening the scientific validity of the enterprise. Blinding thus affects the exercise of power very differently for clinicians and patients. It reinforces the scientific status of the clinical researcher while undermining trial participants who would disrupt the research process. The RCT is inextricably indebted to this power relation.

Despite the esteem with which the RCT is regarded, it is not without its critics. The concerns raised by such critics will be discussed throughout the thesis and will be developed specifically through the case studies in Chapters 4 through 6. But to begin this discussion, consider some of the tensions the RCT creates for the women's health movement and feminist health researchers. As discussed in Chapter 1, feminists have focused a great deal of attention on empowering women

patients and practitioners to challenge and resist the androcentrism which was a prominent component of traditional medical authority. The RCT has the potential to simultaneously disrupt and further entrench gender bias in medicine.

Challenging the androcentrism of clinical trials

One requirement for a successful clinical trial is that it be relevant to those likely to benefit from its findings, so it is important to recruit a study population that reflects the diversity of people potentially eligible for a treatment. However, ensuring diversity in trial populations has not always been a priority and in many instances has not been achieved. Depending on the frequency of the health event in question, in any randomly chosen segment of the community only a small number of individuals will experience the condition under investigation. While these individuals may include women and men from diverse cultural and socioeconomic backgrounds, only a fraction of them will become aware of the existence of a trial, be asked to participate, or be eligible for enrolment. At each stage of recruiting trial participants social factors come into play. Who finds out about a trial and why? Is it because their doctors tell them, they read about it in a newspaper or magazine, or hear about it through radio or television coverage? Once a person becomes aware, how readily can they obtain enough information to decide whether they are interested in taking part in the study? If they are interested, who do they contact and what response does their inquiry elicit? Are they encouraged, or implicitly or explicitly discouraged, from pursuing the matter? The selection process is well underway by the time a study candidate reaches the point of formal evaluation where official screening will further reduce the heterogeneity of applicants. Self-selection and motivation on the part of individual participants is important for the success of a trial, but this commitment from lay participants is

mediated in the first instance by the profile of those approached and invited to participate.

Although technical criteria will govern the biological requirements of the trial, there will be numerous other issues which become the basis for filtering out applicants. When selecting participants consideration is given to whether or not they are able and willing to 'comply' with the experimental regimes in question, as once a person has been admitted to a trial there will be barriers they must negotiate if they are to stay with the trial to its conclusion. For example, are treatments affordable and convenient? Do they interfere with people's daily life, for instance, by causing undesirable physiological changes or by requiring attendance at clinics or time and attention for self monitoring? Do people have the conceptual or language skill to meet the requirements of the trial? Do participants require stable employment and a long-term postal address for adequate follow-up? While clinical researchers may be aware of the goal of getting a representative trial population, they must also select people they believe will help their trial succeed, so the way researchers answer questions such as these shape their choice of participants. By legitimately selecting for success researchers run the risk of assuming only certain types of people are appropriate trial subjects, which in turn may lead to the choice of an unrepresentative trial population. There has been a tendency for trial populations to reflect medicine's belief in a universal body which was both male and white (Dresser, 1992; Keville, 1994). Women and men who differed from this white male norm have historically been under-represented in trial populations.

Questions like those listed above illustrate how the exclusion of certain individuals or groups can be justified by researchers who are seeking to limit confounding variables by constructing a standardised trial population (Angell, 1993: 271). They

also illustrate how attempts to minimise confounders can result in recruitment practices which exclude certain categories of participants and impact on the generalisability of outcomes. Clearly culture and physiology affect how disease and treatments manifest themselves, yet it is the dominant (and largely unquestioned) practice to assume findings based on one gender or racial group can be extrapolated to all humans. But if those who actually complete a trial represent only a small section of the broader community, will the results be meaningful outside the setting of the trial? If the profile of the trial population were predominantly male, is it appropriate to presume the outcome will be similar for women? If the population were predominantly white are the results relevant to other racial and ethnic groups? If the population is predominantly heterosexual is it safe to expect the findings will hold true in the gay or lesbian community? Assuming the worth of a treatment is an increasingly risky business the less a patient resembles the trial population (Assaf & Carleton, 1998), and a consequence of past over-representation of white men in trial populations is that clinicians now lack evidence on whether accepted treatments are beneficial for women or people of colour (Dresser, 1992: 24).

Difficulty in recruiting appropriate subjects has been used as another reason for excluding certain groups from clinical trials (Levy, 1991). As suggested earlier, difficulty in recruiting may be the result of the prevalence of a disease or condition within a given community, however it may be exacerbated by the prejudices of clinicians and the way they design their trials. If so-called design requirements are cited as reasons for the difficulty of recruiting suitable female subjects, an examination of the assumptions clinicians have about the nature of the disease or condition they are investigating coupled with the development of appropriate and

inclusive research strategies, may go a long way towards reconceptualising the profile of potential subjects.

Women's exclusion from research was institutionalised through the US FDA's 1977 policy limiting the participation of women of child bearing age from participation in early trials. The FDA stipulated that, because of the potential risks to a foetus, women of child bearing age should be excluded from the first phase of clinical trials (testing for toxicity and dose tolerance among a small number of people) unless there was the possibility of substantial benefit for the woman involved (as in the case of a life threatening disease) (Wermeling & Selwitz, 1993: 905). These restrictions applied across the board and did not discriminate between sexually active premenopausal women not using contraception, women using hormonal and barrier methods of contraception, those whose partners have had vasectomies, those who were celibate, or lesbians (Merkatz et al., 1993: 295). Although these regulations were relaxed for participation in later phases of clinical trials (as drugs came closer to public release and were tested in larger populations), they resulted in the perception that women do not, and should not, participate equally in trials (Angell, 1993: 271). I would go further to suggest they continue to inform the belief that women are less stable and reliable experimental subjects because of their biochemical difference from male biology, the ethical issues related to effects on foetuses advertently or inadvertently exposed to the experimental treatment, the concern over potential litigation in the face of unknown effects on a foetus, and finally, a perceived difficulty recruiting female participants.

Including women in trial populations is not simply a matter of ensuring they participate in sufficient numbers; it is also a matter of accounting for female

difference from a male norm and somehow standardising the two into a generalisable representation of effects of the drug or procedure under investigation. The multiple forms of female cyclicity repeatedly arise as problematic when comparing treatments among women and men, and when monitoring their impact. For example, fluctuating hormone levels during a lifetime, a menstrual cycle or a contraceptive cycle, or pregnancy, can impact on the actions of drugs so patterns of the effectiveness of a treatment may need to be separately mapped for women at different stages of their lives. In an experimental situation where researchers are attempting to demonstrate a hypothesis clearly and conclusively, negotiating female biology can mean adding an apparently unnecessary layer of 'complexity' (see for instance (Merkatz et al., 1993: 293)). When countering the supposed problems of female difference a number of responses are possible. If homogeneity of a trial population is nominated as important for the smooth generation of an outcome, the question can be asked as to why the trial should be made up of whites and men rather than any other population, for instance Aboriginal and female? The reasons this has largely been the case are ostensively historical and political. In addition, the assumption that female hormones, and not male hormones, complicate research needs to be scrutinised. And why is women's cyclicity considered adequate grounds for exclusion from research populations if women are an ultimate target group for the experimental outcome? If hormones complicate an experimental situation they also complicate the clinical setting, yet perversely in the clinic they have been constituted as a reason *for* medical intervention rather than a reason *against* medical treatment.

In addition to including women in research populations, consideration should also be given to the role their presence plays in analysing whether there are sex or gender related differences in the effectiveness or safety of the experimental

treatment (Merkatz et al., 1993: 924). Even when trial participation is equal amongst men and women and when attempts are made to consider sex and gender as analytic variables there is a tendency to assume it is a variable which needs to be 'controlled' for in such a way that its effects are minimised. For example, Kunkel and Atchley discuss a study of disability and functional limitation among the elderly in which gender was considered as a confounding variable (Kunkel & Atchley, 1996: 294-295). Atchley found that when coded and considered within the trial as a whole, 'gender' was not an indication of functional limitation for aging men or women. When the same analytic models were run separately by 'sex', substantially different findings emerged. Functional limitations in men were not adequately predicted by independent variables such as age, attitudes, and self-rated health. For women, however, old age, a negative feeling about retirement, lower self-rated health, and lower socioeconomic status were significant predictors of ability to function in everyday life (Kunkel & Atchley, 1996). Simply adding women to clinical trials may not produce sex-sensitive outcomes: instead a questioning of individual trial designs and of specific research and analysis methods may be needed.

The specific exclusion of women of reproductive age is based on the need to protect women and their offspring in the instance that a participant becomes pregnant while on a trial (Wermeling & Selwitz, 1993: 908). While fear of miscarriage, birth defects and other foetal damage or pregnancy complications are appropriate reasons for concern, it is worth asking whether they justify the blanket exclusion of all women between the ages of 15 and 50. Beyond the obvious outcome that society cannot be confident of the effects of treatments on women of reproductive age unless they are systematically monitored, this practice assumes that the potential hazards to a foetus outweigh the potential treatment benefits to

women. It also fails to acknowledge that women can make rational decisions about contraception, pregnancy and abortion whether or not they are participating in a trial. This theme is carried into the third reason given for limiting women's participation. In an increasingly litigious climate concerns over damages claims resulting from exposure to harmful medical procedures has been used by sponsors of trials as grounds for exclusion. In the USA, litigation over foetal abnormalities caused by drugs such as thalidomide, bendectin, and diethylstilbestrol have cost the pharmaceutical industry billions of dollars. Since most drugs do not make it past early phase testing, animal studies looking at the effects of a drug on foetuses are normally carried out only when that drug is in later stage trials. It appears to make more economic sense to exclude women from early trials (thereby also limiting liability), than it does to undertake teratogenic screening on all compounds and procedures set for Phase I testing (Wermeling & Selwitz, 1993: 907). Dresser counters this point by arguing that the chance that a few women may become pregnant, might not opt for terminations and subsequently give birth to deformed or diseased babies is not enough to justify the current exclusionary practices. Further, clearly identifying the risk to potential foetuses in consent forms reduces the likelihood that a woman who becomes pregnant and decides against termination will seek compensation. She acknowledges that litigation by any child injured through exposure in utero is not addressed by this precaution (Dresser, 1992: 25-26).

Each of these concerns depicts women's biological identity as centring on reproduction and renders this identity problematic. Because of hormonal cyclicity women are inherently unstable, difficult to understand and difficult to encompass within medical practice. Women cannot be trusted not to become pregnant and pregnancy presents an ethical dilemma which can only be resolved by putting the

rights of foetuses above those of women. Furthermore, if they do become pregnant, women cannot be trusted not to sue pharmaceutical companies. It is safer, therefore, to discourage their participation in clinical trials.

Before leaving this discussion of the gendered nature of RCTs I would like to briefly return to Oakley's work (discussed in Chapter 1). *Who's afraid of the RCT?* is a rare instance of a specific sociological critique of the RCT, which is also explicitly feminist. While many of the concerns she develops are raised by others, she is unusual in articulating them as problems for a feminist health project.

Oakley begins by noting that feminist health research is often pursued by social scientists utilising qualitative methodologies rather than scientists using quantitative methods. She writes that:

> Qualitative methods involving indepth interviewing are seen to be more suited to the exploration of individual experiences - the representation of subjectivity within academic discourse and to facilitate (in practice if not in theory) a nonhierarchical organization of research process... Conversely, quantitative methods (large-scale surveys, the use of prespecified scoring methods, e.g., in personality tests) are cited as instituting the hegemony of the researcher over the researched, and as reducing personal experience to the anonymity of mere numbers (Oakley, 1989: 28).

According to Oakley feminist researchers have been reluctant to engage with quantitative methodologies on the grounds that their benefits may not be attainable without the associated hazards of losing the richness of individual women's life stories and of reducing these women to 'mere numbers'. Yet as women stand to benefit from rigorous evaluation of therapeutic interventions to which they are

routinely exposed, it is necessary to identify potential advantages of the RCT and, wherever possible, separate them from the oppressive influences of patriarchal medicine. Oakley identifies the ownership and distribution of medical knowledge, randomisation and patient and practitioner blinding as particularly problematic for women's health (Oakley, 1989: 29).

Feminist campaigners place importance on validating women's experiences with the medical profession and their own health. As far as patients are concerned, the purpose of blinding and randomisation is to remove individual subjective experiences from the outcome of a trial, which has the effect of placing the interpretation and dissemination of trial outcomes firmly in the hands of clinical practitioners. These practices are, therefore, counter to the feminist goal of empowering women in the clinical setting. For practitioners and researcher, it is assumed that blinding and the random allocation of patients to treatment groups (rather than reliance on professional judgement) is the best way to eliminate potential bias. While this may be beneficial in some instances it can also be read as an explicitly political challenge to the authority of clinicians: the ideological implications of randomisation vary depending on the professional identity of the clinicians and researchers involved and the nature of the medical intervention they are examining. For example, Oakley refers to a midwifery trial which examined the effect of social support on pregnancy outcomes. In this instance it was female practitioners, already operating from a subordinate position to the obstetricians, who were required to relinquish their professional judgement for the process of randomisation.

Feminist challenging of the traditional hegemony of a patriarchal biomedicine, coupled with attempts to redress women's limited employment opportunities

within different levels of the medical profession, has emphasised the legitimacy of the experience of women practitioners. In particular, in keeping with standpoint feminism, it is the experiences of these practitioners as 'women' which partly contribute to a unique form of clinical authority. Requiring they relinquish their clinical intuitions and personal experience as their patients are randomised to different trial groups implies not only that their experiences as (women) practitioners are not a beneficial source of legitimacy, but that they are detrimental to good clinical practice. For many clinicians the move to limit clinical autonomy in a trial setting can be read as a good trade-off as it enhances their status as scientists; for a feminist health researcher, however, it can be read as an attempt to neuter a justifiable source of their authority in the name of a science that has come under sustained attack for being unreflexively masculine.

This chapter has focused on the role of science in medicine by examining historical representations of the RCT and current accounts of different medical research methodologies. My purpose in doing this has been to show that, more than any other form of medical experimentation, RCTs are portrayed as incorporating the rhetorical benefits associated with science and the scientific method. But, as my treatment of the history of RCTs shows, this perception, far from being self-evidently true, has been carefully crafted through a disavowal of the historical and social contingencies that surrounded its emergence and rise to power and continues to surround its use. The following chapter takes up the theme of the scientifically constructed human body and discusses the ways that discourses about sex hormones inevitably refer back to this body and are used to continue the severing of social influences on biology, personality and behaviour.

CHAPTER 3

Constructing the hormonal body

Hormones are historically and culturally constructed entities which are being used to explain an increasing number of phenomena, many of which impact on the meanings of sex. In this chapter I seek to demonstrate how cultural values come to be an integral part of representations of natural biological entities by showing that factors which are not strictly rational and scientific have contributed to the historical development and current explanatory success of hormones. The cultural imagery which is inscribed within scientific accounts of sex hormones illustrates the centrality of hormones in the medicalisation of a range of social phenomena. A consequence of this medicalisation has been an increase in the clinical regulation of these phenomena.

Medicalisation and the sexed body

Sex, in all its manifestations, is a fluid (though deeply embedded) entity whose 'real' and interpretive boundaries are not and cannot be precisely stabilised. Sex is a site of continual contestation in which multiple players vie to define a key unit of meaning, a unit which has been made to speak with authority and conviction to our expectations about life. For instance, sex informs social assumptions about the naturalness of certain psychological preferences of, and physical acts between, consenting heterosexual adults. It speaks to beliefs about the cognitive ability and rationality of individuals and groups. It invokes and continually redescribes aesthetic standards of maleness and femaleness (standards whose redescriptions claim for themselves the status of pre-given).

And these standards are assumed to incorporate two diametrically opposed biological types.

There are many different players seeking to define sex. Problematising 'sex' is at the core of most contemporary gender theory and of the 'body politics' writers such as Elizabeth Grosz (Grosz, 1994), Susan Bordo (Bordo, 1990), Iris Marion Young (Young, 1990), Bob Connell (Connell, 1987), Leonore Tiefer (Tiefer, 1995), and Brian Turner (Turner, 1984). Another key player is biomedicine in its broadest sense. Although biomedicine's primary concern is the codification and stabilisation of biological and psychological sex, a cursory look at the dynamics of medical research and practice shows that medical definitions of sex are also highly contested and under constant revision. Sex endocrinology, the study of sex hormones, is one of the numerous sites through which biomedicine seeks to define sex.

Sex hormones are implicated in a number of phenomena ranging from post-natal depression, to accounts of sex differences in spacio-temporal ability. During the twentieth century there has been a systematic extension of theories and practices relating to sex hormones which enables an increasing number of life-events to be incorporated within the boundaries of medical science through reference to hormones. The notion of medicalisation is a useful tool for understanding how sex hormones have developed within and influenced twentieth century discourses about medicine and sexuality. Medicalisation provides a way of discussing the colonialisation of health, particularly women's health, by hormonal discourses. Theories of medicalisation allow for an account of the genesis and growth of new medical concepts and areas of medical expertise which does not assume a priori that their development and diffusion is

driven entirely by factors internal to the scientific and medical community; that scientific and technological innovation drives the expansion of the profession. By recognising the political nature of medical knowledge and practice, theories of medicalisation also provide a link between attempts to expand medical management of health, and campaigns by both advocates and opponents of specific treatments and technologies. They therefore require an analysis of broader ideological factors by firmly situating medicine within the social sphere. Finally, through this recognition of the ideological and political nature of medicine, they provide scope for linking medical beliefs into the specific production of gender identity. For all these reasons the concept of medicalisation is also compatible with SSK, feminist postmodernism and poststructuralist critiques of the body outlined in Chapter 1. Consequently it provides an appropriate point of entry into a commentary on the meanings of sex hormones in the late twentieth century, and the practices, beliefs, and resistances which have both preceded and emerged because of, these meanings.

Critical discussions about the medicalisation of social life have been a part of sociological theory since at least the 1960s (Pitts, 1968). In 1972 Irving Zola outlined a social analysis in which he described medicine as a major institution of social control (reprinted in Zola, 1983). According to Zola medicine was becoming

> the new repository of truth, the place where absolute and often final judgments are made by supposedly morally neutral and objective experts. And these judgments are made, not in the name of virtue, but in the name of health (Zola, 1983: 247).

The social power of medical professionals has enabled medicine to assume a mantle of truth and moral neutrality which in turn has obscured the manoeuvrings through which medicine has asserted its relevance for an ever-increasing part of social life (Zola, 1983). The negative sentiments expressed here have been taken up by many sociologists who have seen medicalisation as a cumulative project which aimed at social control of deviance according to the requirements of a ruling elite (see, for example, Ehrenreich & English, 1976; Illich, 1977; Oakley, 1984). The way that menopause has become defined as a hormone deficiency disease and its management claimed as the appropriate preserve of the medical profession is one example of how specialists have expanded their expertise to incorporate an area of human life not previously considered as a medical problem (Bell, 1987). Other notable examples include the medicalisation of mental illness (Szasz, 1961; Szasz, 1970), hyperactivity (Conrad, 1975), homosexuality (Bayer, 1981; Stevens & Hall, 1991), alcoholism (Fingarette, 1988; Roman, 1988), body weight and eating disorders (Brumberg, 1988; Riessman, 1992).

In the last decade, theories of medicalisation have developed so as to recognise networks of power and resistance that extend beyond the boundaries of the medical profession. For example, Broom and Woodward argue that it is inappropriate to describe medicalisation simply as a process of medical hegemony controlled and directed purposefully by medical professionals for their own ends. Medicine is made up of relationships among different subcultures within the profession and interest groups within the broader community, some of which can benefit from the clinical and symbolic implications of medicalisation (Broom & Woodward, 1996). An example of this might be PMT or PND which 30 years ago were generic 'women's problems'

whereas now sufferers can gain some solace from being able to name, and possibly treat their problem. Markle and McCrea's study of the prescription patterns of hormone replacement therapy for menopause during the 1970s and early 1980s in the UK and the USA provides another example of the way that problems move into and out of the medical domain, or sit precariously on its boundaries, being subject to pressures both within and external to biomedicine for a redefinition of meaning, treatment and management. They found that national health structures and consumer and feminist pressure groups, as well as medical professionals, influenced what constituted the 'problem' of menopause and the different degrees to which it was considered a medical issue. While feminists in the USA were lobbying against the over-medicalisation of menopause, feminists in the UK were actively campaigning to gain recognition of and medical treatment for the symptoms experienced by many menopausal women (McCrea & Markle, 1984).

Peter Conrad writes that:

> [m]edicalisation consists of defining a problem in medical terms, using medical language to describe a problem, adopting a medical framework to understand a problem, or using a medical intervention to 'treat' it (Conrad, 1992: 211).

Being endowed with the social and cognitive authority to define the nature of problems is crucial because articulating what is problematic or deviant both in terms of biological and social behaviour also serves to constitute what it is to be 'normal' (Riessman, 1992: 125). According to Conrad and Schneider the definition of a problem as 'medical' happens on three levels: conceptual, institutional and interactional (Conrad & Schneider, 1980). On the conceptual

level, a medical vocabulary or cognitive framework is used to define a problem. This may occur in an elite medical literature governed by a small number of influential individuals and it need not involve large numbers of medical practitioners or focus on specific treatments. Consider, for example, how the reconceptualisation of menopause as a deficiency syndrome has contributed to its medicalisation. Theories explaining the mechanisms by which oestrogen deficiency occurs have been investigated and discussed at great length in professional journals using esoteric specialist language. Once a phenomenon has been reconceptualised, medicalisation can take place at an institutional level. This occurs when organisations adopt a medical approach to treating a condition. The shift in the conceptualisation of menopause has been reified in an institutional reordering of medical practice and research which recognises professionals specialising in the menopause and awards grant money accordingly. Other institutions have also incorporated medicine's definition of hormone deficiency disease; for example consider the state reimbursement for menopausal hormone replacement therapy. Medicalisation on an interactional level occurs as part of doctor-patient relations when physicians and patients define a problem as medical or manage a 'social' problem with a medical treatment. The valorisation of women's experiences in the face of medical definitions has been a prime concern of second wave feminism, however the ways in which women take up medical categories to frame their experience and translate that experience into symptoms have resulted in western women's subjective experience of menopause being thoroughly shaped by reference to hormones (Hunt, 1994). In an interaction in a doctor's surgery a conversation between a middle aged woman and a practitioner which once may have referred to a questioning of self and others as the woman faces changing social roles (for

example, role loss as children leave home or contemplation of impending old age) may now refer unquestioningly to balancing hormone levels so as to minimise the detrimental effects of a chemical transition through the menopause.

The construct 'hormone' has been reified within biomedical literature, beliefs, and practices, so that hormones are now considered as real natural entities which exert agency within the biological body. The hormonalisation of health is an ongoing process which involves an expansion of and contestation over beliefs about the nature and function of hormones and their impact on people's lives. It has occurred on each of the levels described in Conrad's account of medicalisation, and ideas about sex hormones now inform the fundamental ways individual subjectivity and identity are formed. Furthermore, developing an awareness of the expansion of hormonal discourses within health emphasises the link between hormones and the belief in a universal and codifiable human biology. Understanding bodies in a way which results from the reductionist methods of science, depoliticises and decontextualises them and allows the effects of medical mediation of social norms to be obscured behind the screen of science.

Medicalisation and the history of hormones

Ideas about sex hormones have long and rich histories which are deeply inter-woven in folk beliefs about masculinity and femininity. Nelly Oudshoorn draws on the importance of these histories in the formation of hormones and links them to Ludwig Fleck's account of the role of 'pre-scientific ideas' in the genesis of scientific facts. Fleck writes that:

> ...whether we like it or not, we can never sever our links with the past, complete with all its errors. [The past] survives in accepted concepts, in the presentation of problems, in the syllabus of formal education, in everyday life, as well as in language and institutions. Concepts are not spontaneously created but are determined by their 'ancestors' (Fleck, 1979: 20).

It is naive, Fleck argues, to think that we can arrive at a 'fact' simply through observation and experiment. Both natural phenomena and current research techniques have a history, and traces of these histories can be found in their modern manifestations. As I have argued in Chapter 2, the presentation of the history of medicine affects our understanding of the scientific knowledge and practices utilised by the profession and the biological organisms with which they concern themselves. Narratives which show that medical knowledge and practice are not geographically or historically fixed, suggest that it is possible to bring about a shift in the way that science and nature are classified and perceived. Fleck argues that it is possible to dispense with the 'natural status' of a phenomenon and to speak instead of "symptoms and states, of various patients and incidences" (Fleck, 1979: 21). To do this focuses attention on how 'symptoms', 'states', 'patients' and 'incidences' have been defined as meaningful, rather than assume there are pre-existing standards against which to measure these categories. In Chapter 2 I showed how the effort to classify appropriate patients, physical states and symptoms created a major problem for clinicians involved in the Co-operative Clinical Group's trials of venereal disease. Similarly, the various and competing identities which sex hormones have assumed during the nineteenth and twentieth centuries show that the formation and deployment of a concept involves an alliance of historical and

contemporary entities in the creation of meaning. Further, they support the contention that the currently held scientific theories do not constitute the essential, definitive, or only possible solution to the questions those theories are asked to answer (Fleck, 1979: 21-22).

Fleck describes the process whereby 'somewhat hazy', 'proto-ideas' which can never be substantiated develop over time, becoming more substantial and precise, until they become foundational elements of scientific theories (Fleck, 1979: 23). While the first identifiably 'scientific' research which can be linked directly with theories of sex hormones occurred in the late nineteenth century as investigations of the substances dubbed 'internal secretions', this work was not the beginning of the sex hormones story. Oudshoorn argues that beliefs about sex reaching back to Aristotle were fundamental in informing the early research on hormones (Oudshoorn, 1994:17). The proto-idea of relevance here is the reference made in ancient literature to sex organs as sites of a vague and mystical power which was not strictly limited to their role in reproduction but also involved the formation of the essence of woman and man. In *A History of Endocrinology* Victor Medvei describes debates about the nature of generation among Greek natural philosophers (Medvei, 1983). The Pangenesis theory held that both female and male seed were formed in all parts of the body while the Hippocratic theory held that the brain and/or the marrow were the site of the generation of seed and that the testicles and ovaries were only storage areas for the seed which came from elsewhere in the body. Two different theories of sexual differentiation were that firstly; the right testicle and 'right womb' produced male offspring, and the left testicle and left womb produced females; and secondly, the more heat produced in the womb, the greater the chance of a male offspring, while a cooler womb signified the likelihood of a female

offspring (Medvei, 1983: 46-66). For Aristotle the soul, the form and active principle of living beings, originated in the male seed while the woman contributed only the rude unformed matter (Schiebinger, 1989: 178-79).

From the Middle Ages to the end of the nineteenth century farmers throughout Europe practised the removal of the ovaries in domestic animals in order to increase growth and strength, and as a means of contraception. This custom was firmly rooted in contemporary folk beliefs about the powers of the sex organs (Medvei, 1983: 46), which again can be traced back to the writings of Aristotle:

> the ovaries of sows are excised with the view of quenching in them sexual appetites and of stimulating growth in size and fatness (from History of Animals, as cited in Oudshoorn, 1994: 17).

Although Medvei does not use the term, he evokes dozens of historical snippets which lay the groundwork for his belief that 'proto-ideas' about sex hormones have always exerted an influence on the human body. For example Greek and Roman healers were said to have used mixtures made from goat or wolf testes as sexual stimulants, a practice which was revived by Western European physicians during the seventeenth century. Early scientific reformers, such as the sixteenth century physician Paracletes, used extracts from animal testes in the treatment of 'imbecility of the instruments of generation'. Another example is the tale of Albert von Bollstadt (1193-1280) (known as Albertus Magnus) a Dominican monk who taught in Paris and Cologne and eventually became Bishop of Ratisbon. Albertus believed in the power of the sex organs, and recommended powdered testis of hog mixed with wine as a remedy for male impotence and sexual weakness, and a mixture of powdered womb of hare in wine as means of increasing fertility in women (Medvei, 1983: 97).

In 1676 the official pharmacopoeia of the London College of Physicians included references to the administration of extracts of animal reproductive organs as treatment for various illnesses and sexual complaints, however by the eighteenth century the physicians of a newly enlightened Europe officially dismissed such practices as quackery. The dominant scientific view was that the primary cause of most bodily action was the exercise of nervous stimuli (Borell, 1976), which meant there was no rational basis for administering these extracts. Amongst the folk healers and within the popular wisdom of the time, however, the practices persisted.

Such stories have become part of our modern cultural history and they can now be recounted with little regard to their original form or meaning. By selectively choosing anecdotes from the vast cultural resources, the sex organs can be thus historically linked with spirituality, the mystery of reproduction and the generation of life, as well as the control of sexual differentiation. This process has also allowed the storytelling surrounding modern masculinity to create a deep and extensive historical connection between the testes and masculinity by linking the testes with longevity, bravery and male sexuality from the beginnings of western culture. This tradition has produced a cultural intuition from which it does not make sense to seek an explanation of the role of male genitals in the formation of masculinity as they are so firmly constituted as an essential and unavoidable biological element of male behaviour.

A point which can be used to delineate the modern history of endocrinology is the late nineteenth century work of Charles-Edouard Brown-Séquard who brought the belief in the potency of the gonads out of the scientific wilderness. In April 1891 Brown-Séquard and his assistant Arsène d'Arsonval presented

findings to the Society of Biology in Paris suggesting that animal tissue contained powerful substances which were essential to the maintenance of good health. They argued that experiments wherein purified extracts from animal organ tissue were given to patients suffering from a number of conditions should supply the evidence for the existence of substances they called 'internal secretions.' If treatment was successful they believed this would prove that the condition was caused by an inadequate production of an internal secretion (Borell, 1976: 235).

Treatment with animal organ tissue became known as organotherapy. Brown-Séquard had originally proposed organotherapy in 1889 when he argued that the testes produced a 'dynamogenic' substance which might be removed from the testicles of animals and injected into elderly or declining individuals in order to restore their strength and sexual performance (Borell, 1976:235). His investigation of the effects on male virility of administering extracts from animal testicles was both flamboyant and controversial but managed to spark the interest of clinical researchers. Borell writes that within weeks of Brown-Séquard's publishing this work, "testicular extract was being given to patients with every kind of illness" (Borell, 1976: 301). A fad of organotherapy sprang up over the next two years so that not only the testes but all organs of the body were thought to possess some kind of essence which could be put to therapeutic use. On the whole, the scientific community responded sceptically to Brown-Séquard's work. His research contravened social taboos around sexuality and could not be theoretically justified, appealing instead to beliefs and practices which were considered the province of old wives tales and fair ground healers (Borell, 1976: 301; Oudshoorn, 1994:18). At the time Brown-Séquard was a medical doctor working at the Collège de France and was the rival and

successor to Claude Bernard an eminent medical scientist, Professor of the Collège de France, member of the Académie Francaise, and first to use the term 'internal secretion' in relation to his work in the 1850s (Medvei, 1983: 7, 709). He was not, therefore, without professional standing. Although considered contentious by his colleagues, his work complemented contemporary Victorian ideas about masculinity and his hypothesis that the 'potent secretions' from the testes made their way into seminal fluid was compatible with the notion that loss of semen (through sexual intercourse or masturbation) depleted men of vital energy (Oudshoorn, 1994:18). He believed that this occurred because testicular secretion provided a vital nutrient to the nerve endings. Retention of semen supposedly ensured adequate nutrient reached these nerve endings, resulting in high levels of the nervous energy which was, at the time, thought to be the major catalyst of bodily motility (Borell, 1976:235). Because of this belief Brown-Séquard argued that withholding or abstaining from the release of semen should produce an increase in a man's strength and energy (Oudshoorn, 1994:18).

At the beginning of the 1890s the body was still understood as being controlled and motivated by the nervous system: indeed, until particular bodily responses arose that could not be explained by nervous control, there was no need to look at internal secretions as being causally linked to biological function (Borell, 1985: 10; Oudshoorn, 1994: 16). The first of these substances to be identified was secretin, which was isolated in 1902 (Medvei, 1983: 340). Once secretin (a fluid excreted by the internal mucosa which triggers a discharge from the pancreas) was isolated, research suggested that chemicals as well as nerves might invoke a physiological response. Conceptually nebulous in the early stages, the term 'internal secretion' referred to a hypothetical biological agent

which was necessary for health and well-being. This substance was noticeable mostly because its absence was said to result in disease. 'Hormone' on the other hand, was more precisely defined and referred to a chemical originating from animal tissue which had specific physiological effects (Borell, 1985:5).

Prescientific ideas about the ovaries as the seat of femininity were incorporated into the theory of internal secretions as changes were taking place in clinical gynaecology (Oudshoorn, 1994: 18-19). For several thousand years it had been assumed, within western intellectual history, that women had essentially the same sexual organs as men except that women's organs were inside rather than outside the body. The womb was known and described long before the ovaries were understood, and by the late eighteenth and early nineteenth century it was still unclear that the ovaries had been named and identified as a female sex organ (Gallagher & Laqueur, 1987: 2). From the middle of the nineteenth century, medical researchers began to focus on the role and functions of the ovaries. Gynaecologists in particular paid increasing attention to the ovaries in the belief that they were responsible for a wide range of conditions affecting women's health and well-being (Gallagher & Laqueur, 1987: 27) The shift from viewing the uterus as the primary site of female sexual formation to seeing the ovaries as fulfilling this function also provided the gynaecological profession with a 'paradigm specific' organ. The further development of sex endocrinology during the early decades of the twentieth century was crucial to the professional delineation of the boundaries between gynaecology and obstetrics (Oudshoorn, 1994:19).

As the theory of internal secretions became more widely disseminated gynaecologists were able to use it to argue that it might be applicable to the

ovaries. The nineteenth century practice of removing women's ovaries as a cure for hysteria, epilepsy, nymphomania and other 'nervous disorders' (Russell, 1995: chapter 1; Scully, 1980: 49) allowed gynaecologists to witness first hand the effects of the procedure. Observing changes in women following removal of the ovaries could be productively combined with Brown-Séquard's theoretical insights; if the ovaries did produce internal secretions then an entirely new mechanism for understanding and treating conditions associated with women's sexual health could be theorised. Based on this premise, gynaecologists argued for a distinction between the ovaries and the uterus which allowed the ovaries to became the professional property of gynaecology while obstetrics turned its attention to the uterus. Linking female disorders to the ovaries by means of these secretions allowed 'women's problems' to became more firmly located within the clinical domain of the gynaecologists (Oudshoorn, 1994: 19).

During the 1890s there was a boom in research investigating internal secretions. This included work on the effects of adrenal extracts on vasopressure, the use of pancreatic extracts to treat diabetes, and the link between the thyroid gland and a number of physical disabilities. Research on the secretions of testes and ovaries formed only a small and highly controversial portion of the total investigations into internal secretions (Borell, 1976). By 1895 both medical practitioners and laboratory physiologists were searching for internal secretions in animal tissue, and clinical and physiological studies were undertaken side by side. The information from these investigations was sometimes contradictory. For instance, extirpation and grafting experiments suggested that the islet cells of the pancreas should produce an internal secretion useful in the treatment of diabetes, however extracts of the pancreas proved ineffective in addressing the symptoms of diabetes in either humans or experimental animals. Likewise,

while the physical changes following the removal of the testes or ovaries suggested that the gonads might produce internal secretions, many physicians remained sceptical about both cures involving oral admission or injection of extracts of animal sex glands, and the existence of a physiological mechanism that could explain their effects (Borell, 1976: 267).

The first person to use the term 'hormone' was Ernest H Starling, professor in physiology at University College in London. In 1905 Ernest Starling wrote:

> These chemical messengers… or 'hormones' as we may call them, have to be carried from the organ where they are produced to the organ which they affect, by means of the blood stream, and the continually recurring physiological needs of the organism must determine their production and circulation through the body (Starling, 1905, quoted in Oudshoorn, 1994: 16).

In the first decade of the twentieth century the study of hormones evolved into the professional domain known as endocrinology. According to Long-Hall and Glick, endocrinology could not then or now be considered a 'discipline'. They suggest instead that from its origins endocrinology has always been a multidisciplinary field which, while strongly influenced by clinical experience, has been dominated at different times by different disciplinary interests (Long-Hall & Glick, 1976: 229). For example, the notion of sex hormones served as a theoretical catalyst to draw together previously disparate research about sex and sexuality. In comparison to gynaecologists, who specialised in sexual medicine, physiologists, who worked with the whole body, were relatively slow to appreciate the importance of the theory of internal secretions to the sex glands. One explanation for this was the taboo surrounding human sex and sexuality.

Furthermore, the controversy over Brown-Séquard's work on increasing virility had sensitised researchers and clinicians to the need for discretion, propriety and adherence to the highest standards of scientific inquiry if the emerging area of sex endocrinology was to be taken seriously. Because of the cultural sensitivity to issues surrounding sex "[p]hysiologists who took up the study of ovary and testes preparations did so cautiously, avoiding association with these therapeutic claims" (Oudshoorn, 1994: 20).

The emergent tension between the clinical applications of the new hormonal theories and their development within the laboratory was a significant factor in the early formation of endocrinology. The existence of internal secretions, although implied by clinical observations, could not be rigorously proven within the clinical process. While trying to determine their nature, laboratory scientists and clinicians initially found it difficult to agree on which organs produced internal secretions (Borell, 1985: 5). Prior to the turn of the twentieth century the ovaries (particularly in relation to 'female ailments') had been the concern of gynaecologists. With the development of theories of sex hormones physiologists had reason to link female disorders with laboratory practice. In so doing, the professional boundaries which divided gynaecologists and physiologists were redefined to create an ongoing interdependence and tension between the two disciplines (Borell, 1985; Oudshoorn, 1994: 20). Gynaecologists were interested in the relation between the ovaries and various disorders they believed were due to ovarian dysfunction. Physiologists, on the other hand, had a broader interest in the overall impact of the ovaries and testes on bodily development.

The acceptance of the hormonal theory in the biological sciences was fostered by the way it complemented a major debate about the sexual development of organisms which was raging in the early years of the century. The resolution of this debate and the way sex hormones facilitated it will be discussed shortly. Michael Callon describes a process of 'enrolment' wherein different theories, technological artefacts or processes "enrol a mass of silent others from which it draws its strength and credibility" (Callon, 1987: 96). These entities are made strong as they position themselves in relation to other accepted or perhaps contentious beliefs, objects and practices. The constellation of relationships between entities "is durable not only because of the durability of the bonds between the points... but also because each of its points constitutes a durable and simplified network [of beliefs, objects and practices]" (Callon, 1987: 96). In the early years of the twentieth century hormonal theories were enrolled by, and themselves enrolled, physiologists and geneticists who were debating the origin of sexual differentiation. Physiologists were arguing for sexual differentiation mediated by environmental and physiological conditions during gestation, whereas geneticists believed that sex was set at conception by a central agent which would later become known as the sex chromosomes. The theory of sex hormones seemed to offer a means of resolving this impasse as hormones could provide an environmental means of effecting the 'intention' of the sex chromosome. Geneticists could retain control of the study of sex determination – the establishment of internal conditions which lead to the development of one sex or another; and sex endocrinologists could control issues of sex differentiation – the development of sexual characteristics over the course of an individual's life (Oudshoorn, 1994:21).

By 1910 prescientific ideas about the gonads being the agents of sex difference had been converted within physiology and gynaecology into a belief that sex hormones were the chemical messengers of a dualistic sexual identity, a belief which has proven to be remarkably resilient. In the early years of the century work on sex hormones affirmed existing commonsense beliefs that the gonads were the source of masculinity and femininity. By focusing on the secretions of the gonads rather than the gonads themselves, however, endocrinologists participated in a gradual cultural reformation of ideas about sexual origin. Prior to 1920 it was thought that there were only two sex hormones which corresponded with two sexes; the female hormone was thought to originate in the ovaries and the male hormone in the testes. This view was an extension of contemporary Victorian ideas about sexuality wherein sex was a strictly dualistic entity (Oudshoorn, 1994: 22). Female and male were seen as two distinct and diametrically opposed categories, and this opposition was not just biological, but dominated the social world as well. This 'sex antagonism' found support amongst the work of sex endocrinologists in the early years of the twentieth century. While earlier work such as that of Brown-Séquard suggested only that sex specific hormones were responsible for sex specific characteristics, later writers argued that each sex hormone was responsible not only for the promotion of the appropriate sexual characteristics, but actively suppressed the characteristics of the opposing sex (Oudshoorn, 1994: 23). This reinforced a distinction between the sexes and allotted certain behaviours and social roles to men and women. In this model, women were defined as being tied to the process of biological reproduction which, by the turn of the century, had been thoroughly medicalised; constituted as inherently pathological, and requiring supervision from the medical profession (Poovey, 1987: 143-145).

The 1920s saw a breakdown in this rigid sexual duality and in the belief that sex hormones are entirely sex specific in origin and function. Later research indicated that both female and male sex hormones were produced by both sexes, and that rather than a single hormone for each sex there were a number of such hormones. Despite this, coding of hormones as male and female has persisted and the association of gendered attributes with the sex hormones continues. In addition, new techniques for the extraction and synthesis of hormones pointed the way towards the widespread therapeutic use of hormones which has occurred in the latter half of the twentieth century.

In the remainder of the chapter I focus on the role of hormones in sexual differentiation of the foetal reproductive tract and brain. My reason for doing so is to highlight that from the moment of conception hormones are being used to establish a relationship between biology and behaviour which normalises certain types of physiological and psychological development. Thus hormones are established as entities which can be mobilised into biologically determinist arguments to account for the social stratification of the sexes and the marginalisation of those who in some way transgress the boundaries of the sexual order.

Prenatal hormones and sexual differentiation

There is a broad consensus among scientists that biologists have a technically accurate knowledge of the development of the foetal reproductive system in humans (Longino, 1990: 115). Sexual differentiation is thought to be determined at the point of conception by the X and the Y chromosome. The sex-determining information from the genes leads to the subsequent formation of either ovaries or testes in what, to that point, had been a bi-potential embryo

(Gordon & Ruddle, 1981: 1265; Naftolin, 1981: 1263). By causing gonadal differentiation the genes are responsible for structural features of the sexual development and function of the body (Haseltine & Ohno, 1981; Naftolin, 1981: 1263) however successful differentiation requires exposure to hormones. Human embryos of both sexes are believed to share the same developmental path until the end of the second month of gestation when the effects of prenatal hormones begin to appear and sexual differentiation occurs. Research into prenatal hormones seeks to identify the specific nature of these foetal hormones and the precise mechanisms by which they affect the process of sexual differentiation and development. Investigation includes examining the stage at which hormone production starts, which hormones are produced and when, and attempting to identify the precise actions and consequences of each hormone.

The effects of prenatal hormones on foetal development were first substantially articulated in the late 1940s by Alfred Jost, an embryologist working at the Collège de France in Paris. Jost was studying the effects of castrating male mammal embryos which he found developed "as female". He explained this by arguing that the emergence of male characteristics happens only if specific hormones produced by foetal testes are present in an embryo. According to Jost's hypothesis (which has become an axiomatic principle of sexual development) the process of sexual differentiation is "sequential, ordered, and relatively simple" (Wilson et al., 1981: 1278). The initial chromosomal sex established at conception determines the development of either ovaries or testes. If an embryo grows testes and produces normal testicular secretions, the resulting hormonal profile brings about male secondary sex characteristics, known collectively as the male phenotype. If ovaries develop or if no gonad is present, "anatomical development is female in character" (Wilson et al., 1981:

1278). Jost's work on foetal castration became the foundation for understanding hormonal control of sexual development. Writing in a special edition of the journal *Science* dedicated to the issue of sexual differentiation, Wilson et al., comment:

> Stimulated by this paradigm, subsequent investigators have sought to identify the specific hormones that are secreted by foetal testes and to elucidate the control mechanisms that regulate the secretion of these hormones at the crucial moment in embryonic development. They have also attempted to characterise, at the molecular and genetic level, the mechanisms by which the testicular hormones act to induce the conversion of the sexually indifferent embryo into the male phenotype (Wilson et al., 1981: 1278).

Several outcomes have resulted from others' attempts to expand Jost's model. To begin with, a research culture was established where, until the mid 1970s, the role of testosterone in sexual differentiation was studied more intensively than the role of oestrogen. In the last quarter of the twentieth century this culture has changed and oestrogen has come to be seen as more significant than previously recognised (Longino, 1990: 115; van den Wijngaard, 1997: 37). In addition, prenatal hormones have been ascribed the cultural characteristics of masculinity and femininity. For example, the above description posits the combination of male hormones as the active agent in sexual formation and the formation of female anatomy as the result of a lack or absence of these (male) active agents. And it is a lack which is substantiated through the experimental mandate of science:

The experimental basis for this thesis involved demonstration that removal of gonads from embryos of either sex prior to the onset of phenotypic differentiation results in the development of a female phenotype. Thus, the male is the induced phenotype in that testicular secretions cause formation of the male urogenital tract where as female differentiation is not dependent on the presence of an ovary (Wilson et al., 1981: 1280).

The very notion of sexual origin was in this way based on a description of female lack and of unequal agency. As the scientific problem of sexual differentiation is considered to be 'closed', it is difficult to suggest that this is not the way it 'really' happens or that this description has in fact resulted from interaction between the process of differentiation and the discourse through which we understand it. Sexual differentiation is seen as a natural pre-given process whose discovery reveals its organisation via male agency and female absence.

The comments by Wilson et al., state that the removal of the male foetal gonads before phenotypic differentiation results in female anatomical development. In addition, it states that the removal of the female foetal gonads also results in female development, confirming feminine passivity. But there are alternative ways of representing the same findings. Consider instead the following description. Rather than describing this as a story of male agency and female lack, could it not describe the natural robustness of the female phenotype? Could it not be argued that in spite of the removal of its gonads a female embryo will develop 'normally', and in spite of the genetic code 'male', without the influence of gonadal hormones the female phenotype will dominate,

resulting in female anatomical development. This hypothetical re-write touches only on the level of representation and seeks merely to demonstrate that sex is not a natural pre-given entity and that alternative readings are always possible. However were it a dominant representation it would be incorporated at a material level into what we know as the process of sexual differentiation.

Organising sex

Once phenotypic sexual differentiation has occurred hormones are said to have either an 'organising' or an 'activating' effect on the body. Sexual determination is the result of the organising effects of hormones while sexual differentiation is said to result from their activating effects. An organising (or developmental) effect is one that occurs during gestation or around birth and establishes patterns which cannot be changed during the life of an organism. It programs biological tissue to respond in specific ways to later events such as the 'normal' development of female and male genitalia (that is, the development of physically dissimilar reproductive organs which are both structurally distinct and which respond differently to various chemical stimuli). Organising effects differ from activating effects in a number of ways. Initially, organising effects occur only during a specific phase of growth and they tend to be permanent although they can be medically managed through procedures such as surgery or hormone therapy. Some developmental effects are dependent on the subsequent activating effects of sex hormones and may not appear until puberty or in adulthood. The way oestrogen levels trigger the release of luteinising hormone during a women's menstrual cycle is an example of an activating function (Longino, 1990: 112).

In *Reinventing the Sexes* Marianne van den Wijngaard provides an in-depth discussion and critique of the organisation theory of prenatal hormones (van den Wijngaard, 1997). According to the original formulation of the organisation theory, proposed in 1959, the presence of androgens causes permanent structural changes in the male brain which directly affect male sexual behaviour (Phoenix et al., 1959). During the 1970s and 1980s the theory was modified to include an active role for oestrogen in the formation of the brain. These hormonally related differences in the brains of men and women have been mobilised to explain differences in behaviour and to justify the continuing social advantages men enjoy at the expense of women (van den Wijngaard, 1997).

Prenatal sex hormones are essential for achieving 'healthy' sexual differentiation but they can also be the agents of profound sexual disruption. Hormonal imbalances during embryonic life can result in problems with sexual differentiation which may become apparent at birth or puberty, and include problems such as 'aberrant virilisation of sexual phenotype', 'dysphoric gender identity' or 'cognitive instability'. Research into the nature, action and effect of prenatal sex hormones in humans has been made possible by the clinical treatment of individuals thought to be suffering from hormonal abnormalities. In other words, conceptualising postnatal hormones as a medical problem has been directly linked to endocrinologists' ability to mobilise the institutional setting of, and interactions which occur within, the clinic. Exposing animal foetuses to sex hormones has been the chief means by which the nature of developmental effects has been explored experimentally. Organisational effects, on the other hand, are usually investigated when children reach puberty or in later adult life (Ehrhardt & Myer-Bahlburg, 1981: 1312). The demarcation between these effects is important because it enables the classification of individual

experiences according to their degrees of difference from an expected norm, while also providing a reference for treating and managing these differences. The treatment of intersex infants is a case in point.

The existence of individuals with ambiguous sexual anatomy, genitals that cannot be easily identified as male or female, has been documented throughout history (Dreger, 1998; Kessler, 1990: 3). While it is difficult to establish the frequency with which intersexuality occurs in the population, according to Anne Fausto-Sterling as many as 4 per cent of births are of intersex infants, indicating that the boundaries between female and male phenotypes are somewhat flexible (Fausto-Sterling, 1993: 22). The medical profession's long history of regulating bodies and desires has found ample expression in the regulation of sexual ambiguities (see for example Foucault, 1980). This regulation, once carried out expressely in conjunction with the church and the state (van den Wijngaard, 1997: 3), now takes place in the clinic and the surgical theatre. Developments in molecular biology during the twentieth century have enabled scientists to classify sexual ambiguities as chromosomal or hormonal, and (particularly the way hormones affect a biological organism) again suggests a boundary between the sexes is not strictly determined at conception but may actually shift over an individual's life. Despite this, doctors persist in their "incorrigible belief and insistence upon" the model of two diametrically opposed sexes (Kessler, 1990: 4). As John Money states;

> Ideologically there is practically no place for what is sex-shared or ambisexual. The very term, ambisexual, is seldom used, being replaced by bisexual. Bisexual does not imply that something is shared in common by both males and females, but is used with pejorative overtones to indicate

> that something appropriate to one sex is incongruously manifested by a deviant member of the other sex. (Money, 1988: 52).

Because of the depth of this cultural committment to two sexes, when a foetal hormone condition or other sexual abnormality was diagnosed in an infant in the latter half of the twentieth century that child was likely to be entered into a program of hormonal and surgical management. Although not ill, such treatment is designed to minimise the socially disruptive effects of the experience of ambiguous sexual status, and to allow the child to take up a place in society as a 'normal' heterosexual male or female (see for example Fausto-Sterling, 1993; Groveman, 1998; Kessler, 1990). Whilst the aims of these 'management' policies are humanitarian, attempting to enable people to fit in socially, the assumptions which underlie them (such as the belief that it is preferable to expose a child to the perils of major surgery and ongoing drug therapy, rather than expose them, their family and their peers to the challenge of negotiating their unusual sexual status) remain unstated and largely unquestioned. The clear wish that there be only two sexes and that these be assessed by a heterosexual norm of both biological and psychological sex are not articulated (Fausto-Sterling, 1993: 22).

An example of this can be found in the classification of male foetal abnormalities. As part of his formative work on phenotypic sexual differentiation Alfred Jost argued that two secretions from foetal testes, Mullerian-inhibiting substance and androgen, are essential for normal male development. He believed that either a failure to produce Mullerian-inhibiting substance or an inability of the tissue to respond to the hormone would result in a condition known as 'persistent Mullerian duct syndrome', a condition in

which genetic and phenotypic males have fallopian tubes and a uterus as well as a Wollfien duct (part of an embryonic penis). An externally visible feature of this condition is the failure of the testes to descend into the scrotum (Wilson et al., 1981: 1280). Why is this considered a pathological deviation? Is it because of a physical appearance which does not correspond with a dominant expectation (thus rendering appearance a major determinant of male sexuality)? Is it because the 'genetic potential' cannot be met in expected ways (thus implying the validity of a nuclear model of sexual differentiation)? Is it because of the biological ambiguity of possessing internal male and female reproductive organs (thus highlighting the fundamental transgression of the expectation of a clear-cut model of two sexes)? Is it to do with lowered fertility rates (thus emphasising the role of procreation in the construction of masculinity)? The answers to each of these questions provides a different account of where the boundary around 'normal sex' may lie. The closing years of the twentieth century have seen medical specialists develop an increased tollerance for allowing their patients to live with the ambiguities of intersexuality, however many treatments and the ethical issues they invoke remain hotly contested (Howe, 1998; Wilson & Reiner, 1998).

Organising gender

In the previous section I discussed how the processes of biological sexual differentiation have been represented in terms which were coded with gender, and the medical responses provoked when differentiation did not comply with a strictly two-sex model. The categories of gender assumed in this process are connected to behavioural patterns which have also been attributed to the biological influences of sex hormones.

The study of the behavioural effects of prenatal hormones was originally limited to questions about sexual conduct, but during the 1970s it was extended to include a broader range of human and animal activities (van den Wijngaard, 1997: 62). In their seminal work *Man and Woman, Boy and Girl*, Money and Ehrhardt argued that in humans (and animals) prenatal androgens affect sexual preferences, grooming and the choice of clothing, career ambition and intelligence, and cause an increase in energy expenditure (as measured through indices such as outdoor play, athletic skills and social aggression). Without the stimulation of androgens they held children developed a feminised identity in which doll play and mothering featured, along with a liking for pretty dresses, a lack of career ambition and a generally lower IQ (Money & Ehrhardt, 1972). Van den Wijngaard notes that although Money and Ehrhardt's later work made more modest claims about the effects of prenatal hormones on sexually dimorphic behaviour (including a withdrawal of claims that prenatal hormones affected sexual orientation and IQ), their early work had a profound impact and its influence continues to be felt (van den Wijngaard, 1997: 62).

As an example of research which addresses the link between prenatal hormones and behaviour I will examine a review article by Ehrhardt and Myer-Bahlburg that appeared in the special issue of *Science,* mentioned earlier, dedicated to scientific explanations for the differences between the sexes (Ehrhardt & Myer-Bahlburg, 1981). Eharhardt and Myer-Bahlburg identify four main areas of research into the effects of prenatal sex hormones on gender related behaviour. These are self classification of gender identity (based on the concept of a dimorphic femininity and masculinity), gender-role behaviour (how people adhere to these gender dimorphisms), sexual orientation (as measured by erotic responsiveness to one sex or the other, whether hetero, homo, or bisexual), and

intelligence and cognitive sex differences (such as abilities related to sex in 'normal' subjects) (Ehrhardt & Myer-Bahlburg, 1981: 1314).

The category 'gender identity' is only relevant in humans. While animal models are available for the measurement of sex dimorphic behaviour, sexual orientation, cognition and intelligence, no equivalent animal models exist for investigating gender identity. Ehrhardt and Myer-Bahlburg argue that as development of gender identity depends largely on the process of learning, studies of children who were born with discrepancies between biological indicators of sexual differentiation and the sex assigned to them during childhood are particularly useful for unravelling the complexities of gender acquisition (Ehrhardt & Myer-Bahlburg, 1981). These are usually children who have been comprehensively medicalised; they have been identified at birth and entered into treatment programs. A few have grown up as one gender, only to become the subjects of intense medical scrutiny when they experience changes at puberty which contrast with their original gender formation (Fausto-Sterling, 1993). Ehrhardt and Meyer-Bahlburg claim that gender identification usually follows the pattern of the gender assigned during infancy and childhood. Just as by the age of five most children have assimilated the principles governing their native language, so too have they acquired an identification with one or other sex which has become an essential and intransigent part of their self identity. Because of this, an experience of 'gender disorientation', whereby a girl grows a beard or her clitoris begins to take on the dimensions of a penis, is seen as pathological and disturbing, warranting immediate correction. Ehrhardt and Myer-Bahlburg claim that if an occurrence such as this remains "uncorrected" individuals may develop "gender identity doubt", a situation which may take years to resolve (Ehrhardt & Myer-Bahlburg, 1981: 1313). Such cases can

provide a stark example of the links between prenatal hormones and the psychosocial expression of gendered behaviour.

On a less dramatic scale Ehrhardt and Myer-Bahlburg refer to two studies on children who had surgery and hormone treatment as a result of their ambiguous sexual status at birth:

> In both samples, the behaviour of the prenatally androgenised girls differed significantly from that of the controls in that they typically demonstrated: (i) a combination of intense active outdoor play, increased association with male peers, long-term identification as a 'tomboy' by self and others, probably all related to high energy expenditure; and (ii) decreased parenting rehearsal such as doll play and baby care, and a low interest in the role rehearsal of wife and mother versus having a career. The characteristic pattern was not transient or limited to a brief phase, but was long-term throughout childhood and was not considered abnormal for female behaviour in our culture (Ehrhardt & Myer-Bahlburg, 1981: 1314).

Here are girls exposed to male sex hormones displaying behaviours that are socially defined as masculine. Although it is stated that such behaviours are not necessarily abnormal, the authors nonetheless imply that they are at odds with expectations. What constitutes normal or aberrant activities in each of these areas follows stereotyped gender models (such as those reified by Money and Ehrhardt's early work) wherein boys are active and aggressive while girls are passive and nurturing.

For feminists and others with an interest in the construction of biology and gender these studies, with their unsophisticated deployment of phallocentric

assumptions, are easy and deserved targets for criticism. However their significance lies not only in the findings of any one study, but in the research trends embedded in them, and the way they contribute to a larger range of beliefs and practices and the reification of a dimorphic behavioural model of biologically determined sex and gender. As Emily Martin points out, it is an ongoing challenge to 'wake up' the 'sleeping' metaphors in science, those metaphors which are hidden within the scientific and technical content of texts (Martin, 1996: 40). In an intellectual tradition in which denouncing a study's methodology is a common form of critique, it is also necessary to draw attention to the cultural inscription of such methods. Doing so robs them of their ability to "naturalize our social conventions" (Martin, 1996: 40).

Conclusion

In the closing years of the twentieth century sex hormones appeared as real natural entities and are active players in the manufacture of personal subjectivity, social gender identity and biological sexual difference. Controversies surrounding the role of sex hormones in the definition or treatment of life-events are a familiar part of modern life. In addition to the examples discussed in this chapter, consider the pathologising of women's reproductive functions, beginning with the stories that at puberty girls undergo massive hormonal changes which render them emotionally unbalanced, representations of premenstrual, pregnant and post natal women as ill and irrational, and the definition of menopause as an oestrogen deficiency disease and the postmenopausal woman as lacking an essential element of femininity (see for example Ripper, 1991; Ripper, 1994). In the narratives surrounding each of these, female subjectivity is constituted as biologically determined and

inherently morbid, and that morbidity is the result of hormones. The linking of male aggression to testosterone again mobilises hormones in the construction of masculinity. One final controversy which warrants mention involves debates about the 'feminisation of nature' as plastics break down to produce oestrogen-like substances which wreak havoc with the reproductive capacity of males (be they alligators in the swamps of Florida or baby boys in Denmark). The debate mobilises particularly lurid imagery wherein the uncontrollable consequences of post-industrial society somehow become manifest as a mutant emasculating woman (see for example Cadbury, 1997; Colborn et al., 1996). The meanings attached to these examples, and the numerous other instances where hormonal explanations shape discourses about sex and gender, may appeal to cultural stereotypes, but they also have a foundation within scientific literature.

In this chapter I have sought to describe how hormones were produced as biological and medical entities in the twentieth century. The evolution of sex hormones went hand in hand with the development of medical technologies which allowed for their clinical use. The subsequent expansion of the significance of hormones has rendered them a potent causal explanation for a wide range of biological, social and environmental events in contemporary life. In examining scientific representations of sex hormones, signs of their production can be detected – in particular in the way they have incorporated historical and contemporary cultural assumptions about sex and sexual morality. The next chapter discusses the tamoxifen breast cancer trial and draws out the ways in which it is predicated on ideas about a stable female biology which is constructed as hormonally pathological and in need of medical surveillance.

CHAPTER 4

The Breast Cancer Prevention Trial

Thus far I have discussed how the ideals of scientific realism form part of the foundation upon which biomedicine is based and investigated the link between scientific and medical realism and the historical construction of current accounts of the human body (particularly with regard to the way discourses about hormones have been written into modern biology and psychology). This and the following chapter examine a specific set of RCTs which mobilise both the rhetoric and practice of science in medicine in the construction of the female body through hormonal discourses. These clinical trials examine the effectiveness of the hormonal drug tamoxifen as a prophylaxis for breast cancer.

Background to the trial

The reproductive capacity of women and patterns of menstrual bleeding have been linked with changes in breast tumours since the early 19th century. In 1836 British doctor Sir Astley Cooper reported that the growth of breast cancers sometimes fluctuates with the phase of the menstrual cycle. By the 1890s a German physician, Schinzinger, had reported that breast cancers grew more slowly in postmenopausal women and argued for 'castration' as a means of slowing tumour growth in women who had not yet reached menopause (Donegan & Spratt, 1988: 10; Pearce et al., 1993: 227). In order to explain these observations doctors argued that there was a sympathetic relation between breast cancer and the ovaries, and as the science of endocrinology developed, this relationship came to be described as one based on the actions of female sex hormones. In 1896 Thomas Beatson, a Scottish surgeon, wrote that he had performed oophorectomies on several women and claimed that

this resulted in the temporary regression of their tumours (Beatson, 1896; Donegan & Spratt, 1988: 10). By the end of the 19th century oophorectomy had become an important part of the management of breast cancer, despite being beneficial in only limited numbers of cases and providing only temporary remissions (Pearce et al., 1993: 227). At this time the theory of internal secretions was gaining ground and gynaecologists were beginning to theorise a link between the sex organs and women's well-being. Oophorectomy was also being used as a treatment for female psychosis (Russell, 1995: 49; Scull & Favreau, 1986; Scully, 1980).

During the twentieth century surgical management, radiation therapy and chemotherapy gradually rose in significance to their present status as the primary mainstream therapeutic response to breast cancer (Pearce et al., 1993: 227). Hormonal therapies such as removal of the ovaries and use of drugs based on hormone manipulation play an important part in modern treatment regimes.

Hormone therapy for breast cancer was initially employed in premenopausal women to reduce circulating levels of oestrogen, however, its use has expanded and it is now also thought to be appropriate for menopausal and postmenopausal women. Since the mid 1970s, two major types of hormone therapy have been developed: those based on surgical removal of the ovaries, adrenal and pituitary glands, and medical treatment with oestrogens and androgens. The three major types of medical hormone therapies currently available for cancer treatment are anti-oestrogens; progestins and the aromatase inhibitors; and aminoglutethimide and 4OH-androstenedione which work by blocking oestrogen and oestradiol secretion in the ovaries and adrenal glands (Namer, 1996). Such treatments are typically given as combined hormone therapy or as a treatment to complement

other types of therapy such as surgery (which includes surgical manipulation of hormones through the removal of glands) and chemotherapy.

Tamoxifen and the treatment of breast cancer

Tamoxifen is a non-steroidal, anti-oestrogenic drug first synthesised in 1966 (Legha, 1988: 219) at the Imperial Chemical Industries (ICI) by pharmacologists trying to develop hormonal contraceptives. While tamoxifen was found to be an effective contraceptive in some animals, (De Gregorio & Weibe, 1994: 28) there was evidence that it stimulated fertility in humans (Laurence & Weinhouse, 1994: 122). During these contraceptive trials tamoxifen showed an anti-oestrogenic effect which researchers took as an indication that it might be useful in the treatment of breast cancer (De Gregorio & Weibe, 1994: 27-28).

Tamoxifen was first evaluated for the treatment of advanced breast cancer in Britain in 1970. Following the reported success of the British experiments, clinical trials were begun in the USA in 1974 to study the effectiveness of the drug as a secondary (adjuvant) therapy given in addition to other standard treatment regimes. The use of tamoxifen as an adjuvant treatment for women with advanced breast cancer became common during the mid 1970s and by the early 1980s it was also being used in the treatment of early breast cancer (Ford et al., 1994: 2727; Jordan, 1992: 231). In 1978 ICI Pharmaceuticals began manufacturing and marketing tamoxifen under the under the trade name Nolvadex, thereby committing the multinational's resources to the continued development and use of the drug. In the thirty-odd years of the drug's existence there has been a gradual expansion of the frontiers of tamoxifen therapy until it is now amongst the most commonly used breast cancer treatments in the world (Batt, 1994: 113). Tamoxifen is most frequently used in combination with chemotherapy for women

with breast cancer, although it also used for other forms of cancer, including prostate cancer (Pineta et al., 1995). The precise action of the drug is still under dispute (Legha, 1988: 220), but it is believed that it may block the process of 'endocrine promotion' (Powles, 1992: 1145) by affecting the hormone receptors (Cohen et al., 1994). Tamoxifen is thought to work by binding to the 'oestrogen receptor' sites, a type of protein found in some breast cancer cells, forming an inert complex thereby reducing the stimulating effects oestrogens have on those breast cancer cells. When oestrogen (which is synthesised predominantly by the ovaries) comes in contact with these proteins it binds with the receptors and triggers cell growth. When circulating oestrogen levels are reduced (for example, at menopause or when the ovaries are removed) these receptor-positive cancer cells do not receive as much oestrogenic stimulation. If a drug such as tamoxifen can interact with the oestrogen receptor without causing cell growth, the cell is effectively 'blocked off' from the stimulating effects of oestrogen even when the hormone remains present in the blood. Hence the description that tamoxifen has 'anti-oestrogenic' effects.

There are different types of breast cancers, not all of which are stimulated by oestrogen, and tamoxifen is not as successful in the treatment of cancers which are 'oestrogen-receptor negative'. But that is not the end of the story. Although tamoxifen has been in use for over thirty years it is currently being promoted as a pioneering example of a new class of drug known as Selective Estrogen Receptor Modulators (SERMs), drugs which act like an oestrogen on some tissues while blocking the hormone to others (Batt, 1998: 4). This double identity allows it to maintain anti-oestrogenic effects while mimicking some of the beneficial effects attributed to oestrogen such as lowering cholesterol and preventing bone density loss (Laurence & Weinhouse, 1994: 122).

Sex hormones are essential to the ways in which medical research conceptualises tamoxifen. Descriptions of the drug's efficacy and appropriate use always refer to hormonal factors. For example, in women with breast cancer, tamoxifen is generally believed to improve both 'disease-free' survival and 'overall' survival for those aged 50 years and over (Early Breast Cancer Trialists Collaborative Group, 1992: 6-7). The highest success rates are reported amongst *postmenopausal* women with *hormone dependent*, *oestrogen receptor positive* breast cancer (Bush & Helzlsouer, 1993: 242; De Gregorio & Weibe, 1994: 27). It is not recommended as a standard treatment for premenopausal women with *oestrogen receptor negative* cancers (Clinical Oncology Society of Australia et al., 1994: 17). In addition, if a woman has tumours in one breast, tamoxifen supposedly reduces the risk of a recurrence after initial treatment, and further reduces the risk of developing tumours in the other breast (van Leeuwen et al., 1994: 448). Tamoxifen is considered to be safe and effective, particularly in comparison with other forms of cancer treatment such as chemotherapy, radiation or surgery. Indeed Adriene Fugh-Berman, of the US National Women's Health Network, comments that when put alongside toxic cancer treatments tamoxifen 'looks like a vitamin' (cited in Batt, 1994: 121). For all these reasons oncologists see tamoxifen as an attractive treatment option.

In 1992 a series of RCTs were set up in North America, Italy, the UK, Australia and New Zealand to investigate the effectiveness of tamoxifen in the prevention of breast cancer. The evidence cited above suggests that the rationale for prevention trials is as follows: because tamoxifen is apparently safe, can reduce recurrence of malignancies in the originally treated breast, and reduce the chance of malignancy in the 'healthy' adjacent breast, it might also decrease the occurrence of malignancies in healthy women deemed to be at 'high risk' of developing breast

cancer. A subsidiary justification not widely publicised, was that individual doctors were already prescribing tamoxifen for prevention 'off label' and it was necessary to evaluate this clinical practice (Smigel, 1991: 1212; Smigel, 1992b: 1692). That clinicians were already contravening the recommended guidelines by prescribing tamoxifen for breast cancer prevention is another example of the tension between clinical and theoretical expertise discussed in Chapter 2: by conducting the trial the research community was attempting to rein in and place conditions upon a clinical practice for which they believed there was little supporting evidence. The North American trial was stopped in April 1998, several years ahead of schedule, because the organisers believed they were so successful that it was unethical to withhold the beneficial treatment from women taking the placebo. This early closure, which was criticised by the UK and Australian trial organisers, will be discussed in detail in the following chapter.

The breast cancer prevention trials (BCPTs) targeted healthy women who did not have breast cancer but were considered to be at high risk of developing the disease. The trials were set up as two-armed double-blind RCTs in which half of the women were randomised to receive a placebo and half received the active agent. The regime under investigation involved predicting the likelihood of a group of healthy but 'high risk' women developing breast cancer, then giving women in the treatment group 20mg of oral tamoxifen per day for a period of five years, before calculating whether they have a lower occurrence of breast cancer than women taking the placebo. Each national trial was a multi-centre trial, which was coordinated through a central administrator and research body, yet was carried out in a number of different institutions throughout the three continents. The Australian and New Zealand trial sought to enrol 3000 women but after extending the original two year recruitment period only registered about 1500 participants.

Although administratively autonomous, the findings from the Australian research will contribute toward a larger UK based trial which was aiming to gather a total of 15 000 women (including the Australian / New Zealand contingent). Due to difficulty meeting recruitment targets this number has been reduced to 7000 and in late 1998 enrolment was still ongoing (Pritchard, 1998). The North American trial aimed to recruit 16 000 women (Bush & Helzlsouer, 1993: 235) but stopped when it reached 13 388 (Batt, 1998; Pritchard, 1998).[2] The Italian trial was eventually cancelled because of a high drop-out rate (Batt, 1998).

Taken at face value, the smaller than expected numbers suggest that the findings of the trials may be weaker than anticipated, but the trial organisers have sidestepped this potential criticism by claiming that tamoxifen has a stronger effect than expected which has allowed them to rework their statistical calculations and still achieve statistically significant outcomes with the smaller groups (CancerNet News, 1996). That the trialists were able to do so highlights the flexibility of numerical measures which have been constituted as stable objective tools and the ease with which they can legitimately be altered when the context in which they are deployed changes.

Although the primary aim of the trials was to test the effect of tamoxifen in reducing the occurrence of breast cancer, the drug is also thought to slow the loss of bone density and improve vascular health. Consequently additional goals were included in the trials' protocols. The way these are expressed varies: for instance researchers working on the Italian trial hoped to bring about a 50 per cent

---

[2] The North American trial was sponsored by the National Adjuvant Surgical Breast and Bowel Project (NASBP) and known as the 'Breast Cancer Prevention Trial' (BCPT). The Australian, New Zealand and UK based trial is called the 'International Breast Cancer Intervention Study' (IBIS). My analysis of the trials is applicable to both trials so for convenience sake I refer to both trials under the acronym 'BCPTs'. Where I am referring specifically to one of the trials it will be identified in the text.

reduction in the number of breast cancers reported and a 30 per cent reduction in the incidence of coronary heart disease (CHD), as well as an unspecified reduction in osteoporosis (Vanchieri, 1992: 1555). The North American trial, on the other hand, was looking for a 30 per cent reduction in cancers (Fugh-Berman & Epstein, 1992: 1143) and a 20 per cent decline in the incidence of CHD (Bush & Helzlsouer, 1993: 235). The UK trial aimed to achieve at least a 30 per cent reduction in the incidence of cancers over a ten year period. The trialists believe such a reduction is the minimum difference that would justify using tamoxifen as a prophylactic among the general population (Faulder, 1992: 30). At the time the US trial was stopped organisers were claiming a reduction in predicted cancer incidence of close to 50 per cent (Baum, 1998: 8). While this claim sounds spectacular, it cannot be taken at face value as the means by which it was arrived at requires careful consideration.

Not without dissent

Whilst it is assumed that these RCTs would resolve the question of whether tamoxifen can help prevent breast cancer they have, in fact, been dogged by controversy. This ranges from the question of whether they should proceed at all, to the early closure of the North American trial, and the interpretation of current findings. The major source of contention in the early planning stage was the proposition that the prevention trials would subject healthy women to a potentially toxic drug. The way commentators have articulated this criticism can be divided into two broad types of problems; social and ethical issues on the one hand, and biomedical and technical questions on the other. This in turn facilitates a demarcation among those who are empowered to join in the debate about different aspects of the trials and emphasises the medical research community's belief that

only those who are initiated into the workings of clinical trials and the human body should be allowed to speak about the biological success or failure of the trial. Broader social and ethical debate about the trials may be discussed by those outside the profession, as they are not seen as being of direct relevance to the biochemical question of whether tamoxifen prevents breast cancer. If, however, one adopts a social constructivist position on science it is impossible to maintain a division between 'technical success' and 'ethical appropriateness'. Any line drawn to differentiate instrumental and moral judgments is "artificial, temporary, and convenient to the purposes of the person or group drawing the line" (Cozzens & Woodhouse, 1995: 541). For example, outcomes of the trials make no sense unless we have some means of assessing the social benefits of preventing breast cancer in high risk women. In order to do this one needs to question the role, function and moral obligations of modern medicine; should medicine serve individuals or society? Should it serve governments or the corporate dollar? In the case of the tamoxifen trial researchers are morally obliged to offer individual women 'best practice' on the one hand, while, on the other, they are promoting a commitment to the greater social good by servicing the requirements of the RCT.

The ethical benefits which a successful trial would entail (be they individual or communal) are essential components of the conditions under which it was originally justified. At the same time the technical terrain within biomedical research is crucial to the state of the ethical debate. For example, within modern medicine the idea of a 'risk-benefit analysis' is premised on empirical information which is assessed in conjunction with moral judgements about what research areas are appropriate to prioritise. As this empirical environment fluctuates (with changes in the success rate of a given procedure, the cost or availability of a piece of hardware, or the existence or otherwise of screening technology), so too will the

social and moral consequences of decisions being made. The remainder of this chapter discusses some of the ways in which the construction of technical indicators for 'risk' are contingent on moral and political suppositions, and elaborates how these beliefs are obscured when presented in scientific debate.

The terms 'risk / benefit ratios' or 'risk / benefit equation' are shorthand for referring to the assessment of the risks and benefits of a proposed treatment. The development of risk / benefit calculations is a necessary prerequisite for any clinical trial. Within western medicine the process of developing a risk / benefit ratio will refer to statistical equations derived from assumed characteristics of the treatment, disease, condition or procedure in question. As the criteria nominated for consideration vary, so does the resulting risk / benefit ratio; for example, consideration may be given to a comparison of factors such as the types of studies used to arrive at these relative risk levels, a breakdown of the trial populations, a more precise account of drug dosage, and duration of a treatment. These factors are rarely directly comparable and are usually mediated through some form of statistical analysis which is supposed to reduce the impact of the biases of particular researchers and the differences between the categories which are being compared. But such calculations are meaningless without the ability to form moral, ethical or political judgements about which decisions to prioritise; is it better to reduce rates of coronary disease, or is it instead preferable to reduce rates of breast cancers?

Developing a risk / benefit analysis requires juggling multiple factors which exist in complex relation to each other: 'certainty' in risk / benefit ratios is contingent upon the instance in which it is calculated and is never directly transferable to other instances without some form of qualification. Despite this, the language and

the ideals of certainty are highly prized and feature prominently in the presentation of medical research. Even when researchers are talking about the statistical probability of different events occurring, great pains are taken to represent the probability of those events as exactly as possible. These are formulated by using empirically derived statistical information about the way in which illness and treatments occur. Theodore Porter's comment that 'all science is measurement' (Porter, 1995: 204) emphasises the importance of finding ways of codifying scientists' judgements and assumptions into numerical form, and implies that decision making by numbers, rather than by personal and professional experience, will protect the objectivity and integrity of the decisions being made.

When dealing with accepted treatments the formulation of risk / benefit ratios involves a process of weighing up the statistical likelihood of one event against another where there is an assumed consensus on the frequency with which the different events occur. In experimental medicine, however, there are no definite indications of how the relationship between risks and benefits may ultimately pan out and it is the very possibility of these events that is in question. Risk / benefit ratios are built upon hypothetically generated outcomes which may not eventuate, or which themselves may become the focus of controversy. Further, one of the problems traditionally associated with experimental medicine is that of depriving a patient of the known benefits of an accepted treatment in favour of the questionable (and potentially hazardous) effects of the regime being tested. This deprivation of known benefits to an individual is incorporated into the rhetoric of biomedicine as being a necessary part of the experimental process if the knowledge and practices being produced are going to have any scientific integrity and ultimately produce a deferred benefit to humanity. Risk / benefit ratios and their statistically calculated confidence intervals are never the bottom line when it

comes to working out the safety of a proposed trial. Performing such calculations always involves a loss of information about possible choices and possible outcomes, and resulting equations do not account for the processes through which they were arrived at (Porter, 1995: 44).

The net expected benefit of the tamoxifen prevention trials is defined in the trial protocols as the difference between the predicted beneficial events (ie. adverse events prevented) and the number of detrimental events (ie. adverse events induced) within the treatment group. This net benefit depends on balancing a number of factors. The 'beneficial events' would be a lower than predicted occurrence of breast cancers, myocardial infarctions and bone fractures within the treatment group. These will be judged against an assumption that tamoxifen increases a woman's risk of developing endometrial cancers, liver cancers, thromboembolic blood clots, and a number of other less immediately menacing side effects (Bush & Helzlsouer, 1993: 236). While the trials were being established and while they are being run, the medical aspects of the controversy revolve around specifying entrance criteria, determining the factors that are taken into account when developing this risk / benefit ratio, and the way different events are prioritised and valued when monitoring the risks and benefits. For example, is one tamoxifen-induced death by thrombosis equivalent to one breast cancer death prevented? How many cataracts induced by tamoxifen offset how many fractures prevented? What are the financial implications of the savings on heart disease compared with the expenditure of additional screening needed to monitor women taking the drug? And so on. At the end of the trials the conclusions drawn will be contingent upon how the proponents and advocates negotiate their way through such considerations, and the extent to which those running them can persuade their

critics that they have accurately accounted for potential advantages and problems in their numerical representation.

Defining risk in the BCPTs

In medical discourse 'risk' is used to denote as specifically as possible the likelihood that individuals or groups will experience a nominated health condition. However, this is only one of the meanings the term has taken on and is set against a background in which the identification of risk is a potent form of political critique. In *Risk Society* Beck describes the rise of risk discourse as a consequence of modernisation. As the promises of modernity fail to materialise and as the modernist vision begins to crumble, its hazards come to the fore forcing us to examine values and assumptions previously taken for granted (Beck, 1992: 14-21). Although Beck focuses largely on the meaning associated with environmental risk, his critique applies equally to biological and medical hazards. He states that much of the debate about risk "is still being conducted exclusively or dominantly in the terms of natural science" with the result that social, cultural and political values inherent in the way we conceptualise risk are unrecognised (Beck, 1992: 24). As long as debates remain technocratic and naturalistic the cultural roots of risk can be obscured by the rhetoric of modernism (Beck, 1992: 24-25). For Beck the rise in risk discourse has a social explanation. He describes the articulation of risk as essentially a reflexive process involving cultural reflection, a questioning of current social structures and practices, and the exercise of moral judgements. In the field of health, both researchers and policy makers place great faith in the ability to quantify and evaluate risk, as the construction of risk in the BCPT illustrates. Indeed, medical risk discourse and the rise of the ethos of prevention has provided an important strategy for social regulation in contemporary societies (Petersen &

Lupton, 1996: 19). Regulation has moved from a focus on ameliatory and corrective interventions to the calculation of risk profiles. This allows medical intervention to be justified not simply on the basis of actual concrete dangers, but also on an expert assessment of an increased likelihood that an unmanageable event may occur and that some medical intervention could prevent it. This shift dramatically increases the potential for intervention, since one need not exhibit symptoms of pathology or abnormality, but simply display a characteristic that experts have nominated as a risk factor (Castel, 1991: 288). Moves to quantify a woman's risk of developing breast cancer should be interpreted in this light.

In the late 1980s researchers at the US National Cancer Institute developed a model for calculating individual women's likelihood of developing breast cancer (Smigel, 1992a: 670). The availability of such a model was a necessary prerequisite for a breast cancer prevention trial. According to the team who developed the model, an increased public awareness of breast cancer risk factors and the need to provide valid information to women who were contemplating medical management of their risk through interventions such as mammographic screening or prophylactic mastectomy were the main catalyst for their work (Gail et al., 1989: 1879). They write:

> Increasing public awareness of breast cancer risk factors, such as having a relative with breast cancer, has created a demand for informed counselling of patients at elevated risk. A woman's decision to embark on a program of intensive surveillance with mammography, or even to undergo prophylactic mastectomy, depends on her awareness of the medical options, on personal preferences, and, very importantly, on an individualised estimate of the probability of her developing breast cancer in a defined period. Such an

> estimate is also useful for designing prevention trials in high-risk subsets of the population and in targeting screening and prevention efforts (Gail et al., 1989: 1879).

The above quote implies the authors were motivated by the service-oriented, responsive nature of the medical profession; it is 'individual women' in a collective 'public' who have created the 'demand' for an informed risk model. However, while an individual woman's risk of developing breast cancer remains an abstract calculation, the process of articulating a risk model has material effects on the practice of medicine. Doctors may now use the Gail risk model to counsel against surveillance they consider to be of statistically marginal benefit. However they can also use it to heighten their own awareness of a specific set of potential risks and to identify women who may have been previously unconcerned about their personal risk of developing breast cancer, and introduce them to personal and medical management of that risk. As the BCPTs would not have been possible without a standardised risk model the very existence of the trials is an example of a direct change in the material practices of medicine brought about by the articulation of hypothetical risk.

Deborah Lupton identifies two major types of health risks which are represented in public health discourses: the risks of environmental factors, such as pollution or hazardous exposures (for example, workplace conditions), and risk associated with lifestyle choices, which can be mediated by the self-regulating subject (Lupton, 1993: 426-427). A third type of risk which features in the BCPTs is that of one's genetic predisposition to develop a condition. This is an 'embodied' or 'corporeal' risk which is located within the body of an individual but cannot be controlled by that individual (Kavanagh & Broom, 1998: 438). Through employing scientific

techniques in a systematic manner, health practitioners believe they are able to discern 'rational' means of making decisions about health hazards. Although medical risk is always anchored in statistical probability, in the instance of controversy it is treated as a force whose existence is real and whose impact is certain.

Gail's technique for attaching population statistics to individual bodies was first published in 1989 in *The Journal of the National Cancer Institute*. His model was described in an article titled 'Projecting individualised probabilities of developing breast cancer for white females who are being examined annually'. Its title and place of publication (the official journal of the US National Cancer Institute, a bastion of cancer orthodoxy) reflect something of the professional and political assumptions upon which it has been constituted. The markers considered to signify 'high risk' of developing breast cancer in the Gail model are specifically biological in origin, rather than dietary or environmental. They are calculated on the basis of a woman's genetic make-up, as determined by family history and her lifetime hormonal exposure. A woman's eligibility for the BCPT, and by extension her risk of developing breast cancer, is calculated with consideration of the number and 'degree' of her relatives who have had breast cancer, her age and reproductive history (as measured by hormonal factors such as age at first menarche and menopause, number of children, and contraceptive history). To enter the trials a woman's risk must be equal to that of a 60 or 65 year old (depending on the trial), or four times greater than average (Lancet, 1992: 735, editorial). These markers apply to individuals, not groups. They make exclusive reference to 'white women' despite the repeated calls of the major research and regulatory bodies in the USA for inclusive design and special efforts to encourage participation by 'minority' groups (a call echoed by the organisers of the BCPT). They apply to the self-

regulating medicalised subject who is accustomed to ongoing medical surveillance. And finally they reify breast cancer as a sex specific disease, failing to acknowledge that the disease afflicts men or to consider risk profiles for men. One criticism levelled against the trial organisers is that they have cast too wide a net in their definition of 'high risk'. According to Marcia O'Keefe, a founding member of the Victorian based Breast Cancer Action Group, the fourfold increase nominated by the trialists provides too general an indication of risk to accurately identify an 'at risk' population or to indicate which of the numerous risk factors tamoxifen may help reduce.[3] Further, although articulated as straightforward biological events or probabilities, it is clear these markers of risk are also signifiers of a certain ideological construction of medicine and the medical subject. When the BCPTs began recruiting, the Gail model had not been validated and if the trials are ultimately successful they will contribute towards its acceptance as a reliable standardised tool in the fight against cancer and the further entrenchment of the values it embodies within the clinical setting. But if these values are inherent in the Gail risk model, what effect might this have on the BCPTs?

Entrance criteria

By turning a sociological gaze at any technical aspect of the BCPTs it is possible to tease out a story about the politics which underpin them; the entrance criteria are a case in point. Because the incidence of breast cancer increases with age, women older than 65 in the UK and Australian trials, and 60 in the North American trial, are automatically eligible for entry. For younger women, eligibility is mediated both by age and an assumed strength of a woman's genetic predisposition towards developing breast cancer. If a woman is aged between 45 and 65 she may enter the

---

[3] Personal interview, February 1995.

trial if she fulfils one of the following criteria: she has at least one 'first degree' relative with breast cancer diagnosed under 50 years of age (where 'first degree' denotes mother or sister); a first degree relative who has had breast cancer in both breasts; two first or second degree relatives (where 'second degree' refers to aunts, grandmothers and nieces) who have had breast cancer; no full term pregnancies and an affected first degree relative of any age; a confirmed carcinogenic lump or 'atypical' lump in the breast or a biopsy finding of proliferative disease and breast cancer in a first degree relative of any age.

As premenopausal breast cancer is considered a stronger marker of a genetic predisposition towards the disease, women with relatives under the age of fifty with breast cancer are classified as being at higher risk (where fifty is nominated as signifying a shift in menopausal status). A woman aged between 35 and 44 is eligible if she has a first-degree relative with bilateral disease diagnosed younger than age 40, two first degree relatives diagnosed younger than 50, or a carcinoma established by biopsy. The effects of tamoxifen during pregnancy are unknown so pregnant women or those "at risk of pregnancy" will not be recruited (Clark, 1993: 168). A familial history of male breast cancer or any other type of cancer, do not feature as an indicator of elevated risk. Other generally identified risk factors incorporate specifically hormonal factors. These include an onset of menstruation at age 12 or younger, onset of menopause age 55 or later, and first child after age 30, or no biological children (De Gregorio & Weibe, 1994: Seeger, 1988 #202: 475). All of these refer to a woman's 'lifetime exposure' to female sex hormones.

The entrance criteria listed above construct a woman's risk of developing breast cancer as a question of bodily function and, with the exception of reproductive choices, as the result of the natural pathology of her body which is beyond her

control. The only factor mentioned above which may be within a woman's control is timing of childbirth and number of children borne, and the perfectly rational choice to limit family size or postpone or avoid pregnancy is said to increase women's individual risk. Outside the BCPTs the rhetoric of unfulfilled reproductive destiny features prominently as a potential risk for breast cancer, with early and multiple pregnancies combined with breast feeding being promoted as offering a protective effect (see for example Donegan & Spratt, 1988: 58-59; Kesley et al., 1993). A particularly interesting example of this is the literature on abortion and increased risk of breast cancer. It would seem that pregnancy alone is not sufficient to offer this elusive protection; it must be pregnancy carried to term. Artificial termination of pregnancy exposes the female body to the very hormones which, if allowed to follow their natural path (pregnancy to term), are beneficial but which when left with nothing to do fester and literally become malignant. Women who suffer natural abortion need not fear, however, as this causes a different pattern of fluctuating hormones with which the body is able to cope (Brind, 1999).[4]

Locating risk so firmly in an exclusively biological discourse in which reproductive function is the dominant theme highlights an inability to recognise or consider the way embodied subjectivity affects physical embodiment. In the first instance biological risk categories encourage research which obscures any interaction between biological and social reality; the actions and effects of hormones on breast tissue, something which can be studied in the controlled environment of the laboratory, become the pressing research question, while the

---

[4] The relationship between abortion and breast cancer remains unclear with different studies reporting both an association, inverse association and no association (Kesley et al., 1993: 41). Despite this lack of clear evidence claims of a link continue to surface as an argument against legal termination (Editorial, 1996a: 83-84; Smith & Broom, 1999: 73).

life experiences which may (or may not) influence the production of those hormones and breast tissue (factors which appear to be more difficult to control and account for in a definitive fashion) are sidelined. Addressing similar concerns, Melbourne based women's health activist Mary Draper commented that if giving birth at a young age and breastfeeding truly offers protection, it then follows that the cancer establishment should be exercising pressure at a policy and research level for increased child support, better maternity leave conditions, more adequate breastfeeding facilities throughout the community and a greater availability of quality childcare so that the decision to bear children young does not disadvantage and socially marginalise women.[5] Pursuing (or even acknowledging) such explicitly political consequences of medical research requires that doctors recognise the inescapable nexus between society and biology. Such a move is in direct contradiction to medicine's self-proclaimed grounding in the natural sciences and the claims that grounding precipitates about social disinterestedness and professional objectivity.

Professional interests and the tamoxifen controversy

The hazards identified in the Gail model are not the only threats to the healthy breast. With the strong emphasis on familial history, it is reasonable to speculate that other aspects of family demographics could provide insights into disease patterns as family life is a base for a number of common exposure factors. There is also evidence for the significance of factors such as socioeconomic status, diet and environmental exposures in the occurrence of cancer (Kelsey, 1993; Rimpela & Pukkala, 1987). Why have the trialists chosen to uphold such a negative account of women's agency in mediating risk when alternative accounts are available? A

---

[5] Personal interview, February 1995.

partial explanation can be found in the disciplinary identity and interests of those running the trial.

Although there are opponents and advocates of the trials who are members of the same medical speciality, one feature of the debate is the extent to which the high profile advocates of the trials are specialist oncologists while those opposing them come from a mixture of disciplinary backgrounds and include epidemiologists, economists, other health professionals and social commentators. The design and operation of the trials reflect this and have produced the cognitive and cultural resources of oncologists as the most appropriate tools for addressing the question of breast cancer prevention. Take for example the question raised in the preceding paragraph. Factors such as socioeconomic status, diet, environmental exposures, and so on, exist outside the control of biomedical oncology: they cannot be precisely accounted for, assessed, monitored or altered by the cognitive expectations or disciplinary practices available within that subculture. Should exposure to potential toxins such as low-frequency radiation or food preservatives prove significant, effective prevention lies with policy and regulatory bodies rather than in the medical clinic. Further, acknowledging the importance of these factors poses a threat to the disciplinary and political interests of the trialists by elevating the epistemological and cultural authority of rival professionals. The construction of risk proposed by the prevention trials, on the other hand, appeals to beliefs and habitual performances which have a strong history within the discursive field of oncology. In other words the prevention trials take exemplars from within the area and seek to extend them so as to demonstrate, through reference to recognisable

and well established professional norms, the reliability of their relationship with the natural world (Pickering, 1982: 125-6).[6]

Professional interests operate on a number of levels in any controversy. Consider this statement by Adriene Fugh-Berman, commenting on the fact that oncologists and surgeons designed the trial:

> ... to them tamoxifen is like a vitamin - it's the least toxic drug they deal with... But those of us in preventive health and medicine have different standards about what kinds of things you should unleash onto a healthy population (cited in Raloff, 1992: 267).

In more broad-based public health it is essential that the toxicity profile of any drug used in a preventative setting be extremely low, as the vast majority of those taking the drug will not benefit from its use. It is not at all clear that tamoxifen fits this description. Oncologists are used to consulting patients who are facing an ultimately terminal condition and treating them with extremely toxic substances whose unintended consequences can be far-reaching and debilitating. Critics point out that this has allowed the trialists to have an unrealistically high tolerance for acceptable risks and dangerously low expectations of safety for the tamoxifen prevention trials. According to Fugh-Berman "[w]e're afraid these tamoxifen intervention trials are really going to set a precedent for experiments in disease substitution - a concept we don't like" (cited in Raloff, 1992: 267). Until the drug's long-term safety has been proven the National Women's Health Network, (USA), of which Fugh-Berman is a board member, will object to tamoxifen's use in healthy women. Here the macro-interests of different parties can be seen in

---

[6] For examples of the role of interests in the growth of scientific knowledge see (Barnes, 1977; Barnes & McKenzie, 1979; Bloor, 1976; Cozzens & Woodhouse, 1995)

operation. When crossing the divide between oncology and public health tamoxifen prevention ceases to be a rational option.

Another example of disciplinary interests inherent in the design of the trials can be seen in their reference to hormones as mediators of health and illness. Karen Smigel, a journalist with the National Cancer Institute, writes of the hormonally focused prevention trial:

> Why look to hormones? The genetic and dietary factors that may also play a role in the genesis of breast cancer are not clearly understood or cannot be easily manipulated. But oestrogens and other hormones, the chemicals that make females female, are substances that researchers can and have influenced for years (Smigel, 1991: 1211).

Unlike toxic waste, food quality or work place safety, hormonal risk factors fall within the realm of laboratory based research, and appeal to a bioreductionism by focusing on internal biological agents as responsible for breast cancer. But more than that, they make reference to established tools that cancer researchers "can and have influenced for years". The assumed causal relationship between hormones and the proliferation of cancer cells serves as an exemplar, a communally held model or example (Kuhn, 1970: postscript) within the cancer research community. In addressing the challenge of breast cancer prevention the trialists have modelled their hypothesis on its analogical similarity to a communally taken-for-granted problem solution. In so doing they have imported cultural standards and practices which are already a regular feature of the discipline (Pickering, 1982: 126). These practices prioritise and strengthen the notion that cell proliferation can be responsible for overall health status and subordinate social, political and cultural factors to the processes of biological functioning. In this sense professional

interests operate in the deployment of technical knowledge and expertise so as to appear to be removed from larger political interests, while actually contributing to the destabilisation of arguments offered by the trialists' opponents by rendering critiques based upon alternative explanations illegitimate.

Tamoxifen and its associated risks and benefits are different things to different individuals and groups, and it is the ability to exert one's own definition of the drug and its actions which drives the controversy. In the BCPTs a primary consideration surrounds the question of subjecting 'well women' to the potential risks of an unknown treatment. Should the trials prove successful there is a further concern about treating large numbers of healthy women with the potentially toxic drug for a relatively rare condition. This concern is expressed predominantly as a philosophical or ethical question rather than a political one (see for example Bush & Helzlsouer, 1993; Faulder, 1992; Smigel, 1992b). While every medical experiment involves similarly intractable 'ethical' judgements, the preventative nature of the tamoxifen trial throws this question into stark relief. The women in the trial are currently healthy and symptom free, and the manifestation of any actual disease is only hypothetical. Although tamoxifen is generally considered to be safe and free from significant side effects, this judgement is usually made when considering it alongside other cyto-toxic anti-cancer treatments, many of which wreak a very heavy toll on the body, and with the assumption that a patient actually has cancer. Making a judgement about a treatment option when one is told they have an 'increased risk' of developing a life threatening condition is very different from making such a decision when one is told they have the condition. This makes an already problematic process all the more difficult to decipher.

The perceived 'safety' of the drug, and consequently the way in which it is understood to be 'effective', changes dramatically in accordance with the trial population and disease state under consideration. A risk / benefit ratio calculated when addressing the treatment of advanced breast cancer with tamoxifen will not be appropriate when assessing the treatment of early breast cancer, let alone healthy 'high risk' women. The positions taken up in the dispute about the trials demonstrate the extent to which tamoxifen is differently constituted according to the political and professional position from which it is viewed. For example, for an oncologist tamoxifen may represent the benefits of possible cancer prevention to an individual woman, while for a women's health activist it may stand for the hundreds of women experiencing nausea as a result of the treatment.

When addressing whether a treatment is ethical, it is often assumed that there is a disembodied standard against which one can judge. Beaglehole and Bonita identify four basic principles of biomedical ethics:

> autonomy, the respect for human rights, dignity and freedom; non-maleficence, the principle of not harming; beneficence, the principle of doing good; and justice, the principle concerned with equity, fairness and truth telling (Beaglehole & Bonita, 1997: 137).

These criteria are based on a liberal humanism which assumes the existence of a 'human nature' that should be guaranteed rights, dignity and freedom, as well as the existence of extrinsic criteria by which to judge the benefits or hazards resulting from medical treatment, or the extent to which they reflect an abstract notion of justice. In much the same way that the rhetoric of science seeks to naturalise and universalise the material world, the rhetoric of medical ethics seeks to naturalise and universalise certain moral assumptions, and in so doing, to erase

the connection between decision making in the political sphere and the ethics of biomedicine. The controversy around the BCPTs, however, shows that the question as to whether the trials are ethically acceptable varies according to the forum in which they are being presented and that the factors necessary for a resolution of this ethical debate also vary according to who is speaking and for what purposes. Argument over the ethical acceptability of both the trials and any subsequent use of prophylactic tamoxifen is central to feminist concerns about the trials, but feminist commentary also places issues of ethical acceptability alongside political questions about the treatment of women in medicine and the conceptualisation of female biology and identity. This will be taken up in the following chapter.

In conjunction with the previous chapter on hormones, this chapter has provided a brief history and description of the context in which it was possible for the tamoxifen prevention trials to take place. A detailed account of the aims and structure of the trials, coupled with a discussion of the way the trials construct and measure 'risk', begin to raise questions about the interests which have been and stand to be served by the design and execution of the trials. In particular, 'risk' in the BCPTs has been medicalised. It is constituted as resulting from the pathological effects of female hormones, entities which in other social and medical discourses are described as essential for normal female sexuality and subjectivity. This is not a beneficial medicalisation, as is arguably the case for premenstrual tension or postnatal depression where there is an existing distress which women seek to have validated and from which they seek relief. Instead the only thing that is validated in the medicalisation of breast cancer risk is a woman's fear and her need to self-regulate. The most a woman can do to control her deviant hormones is to start young in having lots of children (all of whom should be breast

fed), or to put herself in the hands of medical specialists who will manipulate her hormones chemically, provided she is prepared to commit herself to the ongoing expense, surveillance (such as mammography, endometrial biopsy) and other potential unwanted effects. The following chapter continues the discussion of the BCPTs and focuses more specifically on the role of scientific literature in controversy in science and medicine.

CHAPTER 5

Representations of the Tamoxifen Controversy

Chapter 4 outlined the origin and organisation of the tamoxifen prevention trials and began an analysis of the impact on the types of knowledge being produced of the actions of various groups with interests in the trials. I discussed the supposed scientific rationale for the trials and argued that, no matter how strong and persuasive it appeared, it did not provide an adequate explanation for their occurrence. Instead, there were numerous political and material reasons for the successful launch of the BCPTs, including the compatibility of their design with the social organisation of certain sectors of the medical profession and its appeal to cognitive and practical traditions within those medical subcultures. The trials also coincided with a historical moment in the women's health movement which saw grass roots activism in the late 1980s and 1990s as women protested against the inadequate treatment of breast cancer and lobbied for more research money and an improved access to quality services (Laurence & Weinhouse, 1994: 14-138).

Chapter 5 extends the discussion of the dynamics of controversies within science by looking in detail at disputed claims about the side effects of tamoxifen. The reason for including this level of detail is to illustrate the form controversy takes in the published medical literature and to demonstrate that almost no aspect of the trials can unequivocally be taken for granted but can instead be challenged through reference to a complex array of subsidiary hypotheses and research. The role of professional and ideological interests in shaping scientific controversies was discussed in the previous chapter. In this chapter published accounts documenting the controversy will be examined in order to draw out how the identity and

interests of the advocates and opponents of the BCPTs are expressed in the literature. This shows once again that there are problems with the practical application of the commonsense assumption that clinical trials resolve medical controversy; as Steven Epstein has shown in relation to AIDS trial, rather than resolving uncertainty clinical trial can become a source of uncertainty (Epstein, 1996: 312).

The Dynamic of Debate in Science

Controversy in science and medicine normally occurs when groups and individuals disagree over rival fact claims. If a disagreement escalates to the point where it involves the attention of a community of specialists, or a number of such communities, resolution of competing fact claims will provoke a diverse range of social manoeuvrings, including questioning a person's or group's right to speak authoritatively about the issue at hand. When this occurs scientific knowledge and procedures become debates about the appropriate boundaries of professional expertise. Negotiating a settlement involves asking questions: Where are the borders between specialist scientific disciplines? Which disciplines are scientific? What practices are scientific? Who is authorised to speak as a scientist? (Jasanoff et al., 1995: 389).

Such questions can be expressed in a number of different forums ranging from routine unstructured interactions in the workplace, through semi-formal exchanges such as written correspondence and conference presentations, to formal peer-reviewed published accounts. At the start of this project I hoped to analyse some of the informal articulations of the controversy through interviewing the organisers and clinical researchers associated with the Australian trial and perhaps to gain access to some of the administrative and historical documentation associated with

it. To this end I approached organisers on a number of occasions during 1995. While attempts to contact consumer and feminist health activists were enthusiastically received, with the exception of Professor Martin Tattersall, a member of the Australian Breast Cancer Clinical Trials Group (the board overseeing the trial), I was unable to gain access to any of those officially associated with the trial. I believe there are several reasons why my requests were unsuccessful. My motive for choosing the trial was based primarily on the way it embodied the application of scientific values in the practice of experimental medicine – the issues raised by a specifically gendered technology aimed at prevention rather than palliation added interest but were not my first concern. I was not initially aware of how politically sensitive the trial was at that time. There has been an unusual amount of commentary about the trial both within the research community and in the broader community, much of which has been critical.[7] As I was unable to gain direct access to the trialists and their account of events, I felt I could not rely heavily on interviews and other personal commentary from people who were critical of the trial. In order to minimise the bias inherent in my own narrative and create some degree of symmetry in my reporting I have limited my analysis of the controversy to publicly available published accounts. Despite this limitation and the convention in scientific writing to erase the social context from which such work emerged, it is possible to use published accounts to explore the social processes of scientific controversy.

---

[7] Following allegations of falsification of data in another breast cancer trial, recruitment had been temporarily suspended in the US in February of 1994, and the MRC in the UK publicly expressed concern about endorsing the BCPT. The consent forms had to be re-written in both the US and UK. In Australia, the ethics committee at Newcastle University also refused the original informed consent forms put forward by the trialists (Dr Paul Craft, Director of Oncology Royal Canberra Hospital, personal correspondence, Saturday 19th August, 1995).

Texts are linguistic mediations of thoughts, actions and experiences, and the use and strategic deployment of textual representations can be a technique for persuading readers about the benefits of one's own position (Jordanova, 1986: 17). They contain information about the genre in which they are written, the relationship between reader and writer and the identity of the author. All of this information contrives to locate the meaning of a text within a set of social relations. In addition, the content of a text also gives insights into what is not being said, or cannot be said within any particular discourse. This in turn reveals much about the conscious and unconscious constraints, models and sources writers employ and the relationship they create between the form and content of their arguments (Jordanova, 1986: 19-20). The act of writing can, therefore, be seen as an attempt to establish a relationship between author and reader, although this can by no means be fully determined by the author. In addition, the act of writing as a 'scientist' makes presumptions about the kind of relationship being established, and the authoritative basis of that relationship. As Jordanova comments:

> To write is to assume a position of authority. To write as a scientist doubles the authority, because an authoritative account of reality is being established. Scientists and medical practitioners who put pen to paper are claiming to 'tell it as it really is' (Jordanova, 1986: 20-21).

Despite tendencies to differentiate between various modes of literature, it is important to stress that scientific texts contain traces of the social context from which they originate. Accordingly, the daily goings-on within scientific laboratories are arguably "the organisation of persuasion through literary inscription" (Latour & Woolgar, 1979: 88). Latour and Woolgar hold that scientific activities are aimed at transforming possible concepts and entities which

must be linguistically justified, into statements of 'fact' which require no such qualification. When this transformation occurs, knowledge claims lose all vestiges of having ever required qualification and appear, instead, to be naturalised within an existing body of beliefs (Latour & Woolgar, 1979: 106). The processes and types of linguistic strategies used to make the context of production vanish is part of the ordering work of everyday science (Law, 1994: 31). While these strategies can never be precisely reconstructed, they can be alluded to through an analysis of scientific texts, so investigating the published scientific papers relevant to a controversy can shed light on the preoccupations and interests of scientists and impacts these have on ways controversy is shaped (Knorr-Cetina & Mulkay, 1983: 10; Pinch, 1986: 31).

In studies of controversy, the tamoxifen debate (in the context of the BCPTs) is slightly unusual because it was not originally the outcome of the experiment which was being contested, but whether the experiment should take place at all. This effectively displaced the emphasis away from the facts produced by the trials onto the facts used to justify the trials: what criteria should be used to draw up procedural boundaries for the operation of the experiment and what criteria should be used to measure and quantify its success or failure? The early closure of the North American trial has shifted this focus back to a debate over the results of the trial. In this chapter I canvass representations of contesting claims about the positive and negative effects of tamoxifen and the strategies used to legitimate those claims.

In 1990 the UK Coordinating Committee on Cancer Research held an international symposium to discuss the conduct of a tamoxifen breast cancer prevention trial. According to the organisers, that one-day meeting thoroughly aired and settled all

relevant ethical issues with the international guest list (all of whom were medical professionals) reaching the conclusion that "the rationale for doing a tamoxifen chemoprevention trial was no longer controversial" (Faulder, 1992: 29). That conclusion proved to be unwarranted. Despite the best efforts of the proponents to make the trials seem like technical and ethical imperatives and to suggest that all the contentious issues had been resolved, the dissent which marked the planning stages of the trials has continued to the present time.

In response to initial proposals, the British Committee on Safety of Medicines officially approved the trial in February 1992 and study leaders began organising recruitment (Lancet, 1992: 735, editorial). The US Food and Drug Administration also approved the trial at this time. On the 12th of March, however, the British Medical Research Council (MRC) withheld its endorsement because of evidence indicating tamoxifen caused liver toxicity in rats and because of the ethical issues involved with giving an anticancer drug to healthy women (Laurence & Weinhouse, 1994: 123; Raloff, 1992: 266). Dr Dai Rees, the secretary to the Council, stated that "the MRC has no wish to spread alarm amongst women taking tamoxifen for proven cases of breast cancer..." for whom tamoxifen "is a well-tried and effective treatment" (Raloff, 1992: 266). But as the trial sought to use the drug in well women it was advisable to proceed with caution pending the availability of adequate research to better inform risk/benefit calculations (Lancet, 1992: 735, editorial). The misgivings of the MRC were mirrored to a lesser degree by the Imperial Cancer Research Fund and the Cancer Research Campaign, both of which maintained provisional support for the trial contingent upon the UK Department of Health re-examining and approving the trial design (Raloff, 1992: 266). This official apprehensiveness flagged growing concerns among peak women's health organisations and sectors of the medical research community as close scrutiny of

the feasibility and accuracy of claims being made by the trialists pointed towards contradictory results. Chapter 4 examined how this concern was directed at the construction of risk and the entrance criteria nominated by the trialists, and claims about the ethical acceptability of the trials. Disagreement also arose over specific elements of the evidence used to justify the trial and its predicted outcomes (both negative and positive).

Contesting claims about effects and side effects: Contralateral breast studies

Initially Fugh-Berman and Epstein criticised the trials by arguing against the reasons used to justify them. Although Fugh-Berman and Epstein acknowledge eight RCTs which show tamoxifen reduces the incidence of contralateral tumours among women with breast cancer by 30 per cent, they believe this did not warrant a chemoprevention trial. Proponents of the trials have assumed that a woman's 'healthy' breast can act as an experimental control when she is given tamoxifen for diagnosed breast cancer. Fugh-Berman and Epstein argue that a reduction in contralateral tumours is not a relevant marker for women who have never had breast cancer since the effects of tamoxifen may hinder the growth of existing but undetected contralateral tumours rather than stop the development of new tumours. As both breasts of a woman with breast cancer have been exposed to identical pathogens, be they genetic, reproductive, hormonal, or environmental, there is no scientific basis for regarding the contralateral breast of a woman with breast cancer as a normal, healthy control (Fugh-Berman & Epstein, 1992: 1143). They also cite evidence that when tumours do occur in the contralateral breast of women taking tamoxifen, they are more virulent and associated with a higher mortality. Using the contralateral breast cancer studies as a justification for the BCPTs produces the

subjects of the trial as breasts removed from women and bodies. The trialists attempt to separate breasts from whole body systems wherein they are the materialisation of a woman's history. In so doing breasts become objects which can be studied in isolation – isolation not only from a woman's life, but also from her other breast.

Conflicting predictions

According to the claims outlined in the North American protocol, if that trial were to have gone to plan, 38 endometrial cancers and up to 13 pulmonary embolisms would have been induced in the experimental population as a result of tamoxifen treatment. These would, however, be outweighed by the prevention of 62 breast cancers and 52 myocardial infarctions (Bush & Helzlsouer, 1993: 236) and by a "significant" increase in postmenopausal bone density (Powles, 1992: 1145). In contrast with these figures, breast specialist Richard Love calculated that in the same trial population there would be 58 breast cancers and 10 fatal and non-fatal heart attacks prevented and a total of nearly 300 unspecified negative events induced (cited in Laurence & Weinhouse, 1994: 124). In a letter to *The Lancet*, yet a different claim appears. According to Nicholson, an American clinician who sought to run a similar trial, 40 cases of breast cancer per 10000 woman-years should be expected among the women with a risk equivalent to those taking part in the trial. Treatment with tamoxifen should reduce this number by 6.6 breast cancers per 10000 woman-years (Nicholson, 1992: 1551).

Producing written representations of a phenomenon is an activity which occurs in a context, and the social orderings favoured by that context are borne out in the resultant text. In the case of a medical research paper or other scientific publication these orderings are likely to include attempts to hide the context of production

(Law, 1994: 31-33). It may be appealing to ask which of the predicted outcomes for the prevention trial is accurate, but it is perhaps more profitable to point out that such claiming and counter claiming demonstrates the flexibility with which statistical data are generated. The source of this flexibility is not specified in the papers cited above but brings to the fore the fact that even when standardised statistical packages are used to predict outcomes and interpret data, judgements must be made about the characteristics of the population and diseases to which they are applied: who is a representative member of any trial population and what are the normal rates at which they will experience a condition? It is part of the mundane work of science to resolve differences about, and gloss over, these judgments. When controversy occurs, strategically targeting an opponent's assumed points of reference highlights and disrupts this seldom acknowledged process and opens the way for debate about those assumptions.

Bone protection

In the previous chapter I discussed how the relative values attributed to the various risks and benefits of the trials remain a source of contention. Negative side effects not considered in the risk / benefit equations include hot flushes, depression, vaginal discharge, and menstrual changes. In addition, the effects of tamoxifen on the eyes are noted in the protocol but were not thought significant enough to include as numerically weighted risks (Bush & Helzlsouer, 1993: 235). The inclusion of claims about the benefits of tamoxifen for hearts and bones has been a crucial element in marketing the positive effects of the trial. According to Fugh-Berman and Epstein, however, the evidence for these positive predictions has been exaggerated. Fugh-Berman and Epstein refer to eight studies on osteoporosis, five of which identified no effect of tamoxifen on bone density. Two of these studies

were retrospective series, (Fornander et al., 1990; Love et al., 1988) and three were prospective investigation (Fentiman, 1989; Gotfredson et al., 1984; Powles et al., 1989). Three prospective studies found tamoxifen increased the bone density of lumbar vertebrae however spinal osteoporosis, unlike hip fractures, is not associated with increased mortality (Love et al., 1992; Turken et al., 1989; Wolter et al., 1988). They also assert that no study has shown a protective effect of tamoxifen on the cortical bone in the femur, or a decrease in hip fracture rates, and it is hip fractures which are responsible for most of the serious morbidity and mortality associated with osteoporosis. Accordingly, the expected advantages of tamoxifen for bone density are actually less than the trialists make them out to be (Fugh-Berman & Epstein, 1992: 1144).

Cardiovascular benefits

The cardiovascular benefit of tamoxifen also comes under scrutiny. Fugh-Berman and Epstein argue that although conjugated oestrogens consistently decrease low-density lipoprotein and elevate high-density lipoprotein (HDLs) cholesterol (with the effect of improving the condition of the blood vessels that supply the heart), the picture with tamoxifen is unclear. It is variously reported to decrease, maintain, and increase HDLs (Fugh-Berman & Epstein, 1992: 1144). Effects of tamoxifen on total cholesterol are also unclear. Most studies have shown a reduction in total cholesterol; however one found no change. Fugh-Berman and Epstein refer to reports that tamoxifen occasionally leads to a striking increase in total cholesterol and triglyceride concentrations. In addition, although the risk for men of cardiovascular disease increases with total cholesterol concentrations over 5.2 mmol/l (200 mg/ 100dl), women's risk does not appear to increase until their levels reach 7 mmol/l. Since low HDL levels are thought to be a reliable predictor of

cardiovascular disease in women, reducing total cholesterol without increasing HDL may not be beneficial. Further, only one out of eight RCTs on tamoxifen reported a decrease in cardiac disease and this finding can be discounted since there is no indication that accurate baseline cardiovascular risk factors were gathered (Fugh-Berman & Epstein, 1992: 1144).

Summarising the data on cardiovascular protection resulting from tamoxifen use, Bush and Helzlsouer reported on one study in which deaths from myocardial infarction among the treatment subjects were approximately half those in the control group. There was, however, no significant difference in overall deaths from other cardiovascular events such as strokes and chronic ischaemic heart disease. They argue that

> [w]hile this finding is somewhat encouraging, there were methodological problems [with the trial] that could have affected the validity of the results (Bush & Helzlsouer, 1993: 238).

After listing several such problems, they concluded that

> [g]enerally, these suggestive but limited findings on the effects of tamoxifen on lipids and cardiovascular events would be insufficient to justify a full-scale clinical trial of tamoxifen use for cardiovascular disease prevention in women (Bush & Helzlsouer, 1993: 238).

Note the recourse to the rhetoric of methodological precision: the research, although suggestive, was methodologically flawed and therefore cannot be considered conclusive. So, again, it would seem that the empirical evidence for the benefits of tamoxifen for osteoporosis and heart disease can be strategically deployed both to defend and criticise the trials.

Endometrial cancer

An elevated risk of developing endometrial cancer is one of the generally accepted effects of tamoxifen use. Because of the association between endometrial carcinoma and unopposed exogenous oestrogen (which emerged in the 1970s among women taking HRT) it is thought that the oestrogenic actions of tamoxifen are responsible for this link (Magriples et al., 1993: 487-488). This aspect of the controversy seems to revolve not around whether there is some causal link between tamoxifen and endometrial cancer, but rather around attempts to define this relationship precisely. Issues which have been raised include the frequency with which women taking tamoxifen develop endometrial cancer, the dose at which cancers develop, and the effects this information should have on calculating risk-benefit ratios for the prevention trials. Nayfield et al cite a fivefold increase in the occurrence of endometrial cancer in women being treated with tamoxifen (Nayfield et al., 1991). Advocates of the trials claim that this increase is on par with that expected in those taking oestrogen therapy at menopause, however critics argue that this is inaccurate given that the prescription of high-dose oestrogen replacement became less common in the late 1970s precisely because of the risk it posed of inducing endometrial cancer (Harlap, 1992; Kaufert & McKinlay, 1985: 117-119). While the risk of developing endometrial cancer might be an acceptable trade-off for a woman facing the recurrence of breast cancer, the same may not be true for a woman who has not had the disease. A tiny change in the perceived frequency rates could have a devastating effect on the success of the trials, as could a shift in the perceived severity of the disease.

This indeed occurred when data relating to the incidence of tamoxifen-induced endometrial cancer prompted the US National Cancer Institute to order clinicians

working on tamoxifen research to rewrite consent forms and ask participants to re-sign them (Seachrist, 1994: 910). Bernard Fisher was chief investigator on a study of tamoxifen therapy for cancer which began in 1981 as well as being a chief investigator with the IBIS prevention trial. In December 1993 findings from Fisher's earlier study prompted his group to send out warnings to all clinics participating in the BCPT to the effect that updated information about the risk of tamoxifen-induced uterine cancer meant that consent forms would require revision. Recommendations for a revised version were sent out on January 14th, 1994. The NCI issued similar advice to doctors using tamoxifen in treatment trials two days earlier (Seachrist, 1994: 910). Following this development the NCI agreed to give 800 of the women in the trial yearly endometrial biopsies so as to obtain more detailed information on the effects of tamoxifen on the uterine lining.

Although oestrogen was first linked to endometrial cancer in 1975 (Zeil & Finkle, 1975), oestrogen induced cancers have been seen as an acceptable risk because on the whole they can be contained by available treatment options. They are described as 'low-grade' cancers because they are comparatively easy to detect and can be treated relatively successfully. It is this understanding of endometrial cancer which has informed the development of the trialists' risk / benefit equation and has led to the belief that a certain number of endometrial cancers are inevitable and are an acceptable trade-off for a reduction in breast cancers. For example, Ford et al, write that tamoxifen

> may cause thromboembolic reactions and endometrial cancer… These risks are small and are clearly outweighed by the agent's benefits in the adjuvant setting (Ford et al., 1994: 2728).

They continue that in the prevention trial

> [i]f tamoxifen use were to double the risk of endometrial cancer and thromboembolic disease, the suggested 33% reduction in invasive breast cancer and the 20% decrease in myocardial infarction still would translate into a significant net benefit for tamoxifen therapy.

Further, Jordan et al, state that

> Metastatic breast cancer is invariably fatal, whereas endometrial cancer is a curable disease. In light of the extensive use of tamoxifen, the overall incidence of endometrial carcinoma is rather modest and is probably less of a concern than is the administration of estrogen to healthy postmenopausal women… (Jordan, 1992: 232).

Critics of the trials responded to the assertion that endometrial cancer is an acceptable risk by questioning the medical profession's ability to effectively manage the iatrogenic consequences of its treatment practices. They point out that it is unrealistic to expect that all endometrial cancers resulting from tamoxifen treatment will be identified and treated successfully. There are margins of error in current detection techniques, and treatment, while comparatively effective, is not free of costs and risks. Further, to assume that cancers will be detected and treated is to assume that women in the trials will be prepared to subject themselves to an additional degree of medicalisation and surveillance by learning to monitor for the appearance of suspect symptoms and by submitting to endometrial biopsy, hysterectomy and other treatments and interventions which are painful and otherwise distressing (Raloff, 1992: 267). But the possible effects of the trials on individual autonomy do not make a strong argument within the logic of biomedicine. The stakes are raised more strategically by opponents of the trials who have put forward the claim that the endometrial cancers induced by tamoxifen

are an unusually virulent hybrid which lack the characteristics of normal endometrial tumours. This new iatrogenic menace, rigorously documented by laboratory and clinical scientists, are 'high-grade' tumours, not as responsive to treatment as 'low-grade' tumours on which the risk / benefit calculations were based (Magriples et al., 1993), so the risks calculated by the trialists are understatements.

Liver problems

The effects of tamoxifen on the liver present another area of contention. Laboratory studies in animals have found an association between tamoxifen and hepatic cancer. Liver cancers occurred in 11.5 per cent of rats fed low doses of tamoxifen, and when exposed to high doses as many as 71.2 per cent developed cancer (Nayfield et al., 1991: 1450). In order to explain and discredit this result researchers have argued that oestrogen receptors in rat livers more readily bond with and absorb oestrogen than do receptors in human livers. There are differences in the way the drug affects rats and humans and although there has only been anecdotal evidence of a link between tamoxifen and hepatic cancer in humans, the possibility has not been ruled out and remains the subject of ongoing attention (Fugh-Berman & Epstein, 1992: 1144).

Existing knowledge is crucial for assimilating and understanding new findings, and according to the dominant view within oncology there is no demonstrated link between liver disease and tamoxifen. Because advanced breast cancer frequently metastasises to the liver, there is the potential for cancer actually caused by tamoxifen to be attributable to the progressing breast cancer. Critics of the trials claim that when a woman receiving tamoxifen develops abnormal cell proliferation on the liver doctors simply assume it is a metastasis. In order to differentiate

between the spread of breast cancer to the liver and new independent liver cancers possibly resulting from tamoxifen, liver biopsies must be performed, but this seldom happens. Here, again, critics are strategically highlighting the shortcomings in current medical management as a way of problematising the assumptions of the trialists. Limited financial resources, time constraints and existing beliefs all work against documenting the possible link between liver cancer and tamoxifen. Aside from cancer, there is evidence that tamoxifen may be associated with other forms of liver disease or damage to liver function. The Committee on the Safety of Medicine in the UK has attributed four deaths to liver failure resulting from tamoxifen use, and has implicated five cases of tamoxifen induced hepatitis, one of which also resulted in death (Ching et al., 1992; De Gregorio & Weibe, 1994: 50). In addition, animal studies have indicated that tamoxifen breaks down in the liver in such a way as to act like a chemical carcinogen rather than to produce the expected hormonal action and further, can cause damage to liver DNA (Raloff, 1992: 268-69).

Effects of long-term use

Little is known about the long-term side effects of tamoxifen as few women have been given it for more than five years. The advent of the prevention trials makes extended treatment likely. While the trials were originally expected to run for five years, a new American trial which began when the NASBP trial was stopped (and is recruiting from its population) will extend tamoxifen treatment for a further five years. And should the BCPTs be considered successful, women will be encouraged to keep taking tamoxifen indefinitely so as to maintain the drug's preventative effects. The fact that women may be medicated for life has not been widely

reported. In my research I have found few references which make this implied consequence of the trials explicit. For example, Ford et al write that

> [t]umor regrowth does occur when tamoxifen treatment is discontinued, indicating that long term tamoxifen therapy may be needed for the continued suppression of breast tumours (Ford et al., 1994: 2728).

And later, while referring to the women on the trial, Ford writes;

> All subjects will be followed for the remainder of their lives (Ford et al., 1994: 2729).

This continued use of the drug adds another layer of concern when considering the long-term implications of the trials, as many questions about extended tamoxifen treatment remain unanswered. In the early 1970s evidence pointed towards a 'conservative course' of one year's treatment because tamoxifen exposure sometimes made tumours resistant to hormone treatment and even stimulated malignant cell growth. The long term effects on the endocrine system were also unknown. Research undertaken during the 1980s indicated that more lengthy treatment is warranted, however there are no clear guidelines as to optimal treatment duration (Saltman, 1994: 7). This raises the possibility that if women are regularly exposed to prophylactic tamoxifen and develop breast cancer, their tumours may be hormone resistant and therefore more difficult to treat (Raloff, 1992).

Eye damage

While tamoxifen has been associated with various eye disorders these problems have usually been linked with significantly larger doses (240mg per day) than

those being given in the BCPTs (20mg per day) [De Gregorio, 1994 #206; 51; Kaiser-Kupfer, 1978 #457]. Despite this, a prospective chemotherapy trial involving sixty three women who received the same dose of tamoxifen as is being used in the prevention trials, found that low dose tamoxifen can also induce eye problems (Pavlidis et al., 1992). Retinopathy resulting from exposure to tamoxifen is not necessarily reversible when treatment stops. As mentioned earlier, eye problems were not included in the trialist's risk / benefits equations and were not prioritised as a source of controversy when the trial was being established (Fugh-Berman & Epstein, 1992: 1144). When the North American trial was stopped trialists found a statistically significant increase in the number of women taking tamoxifen who developed cataracts (574 vs. 508), while the number of those opting for cataract surgery among the tamoxifen group was nearly twice that of those taking the placebo (114 vs. 73) suggesting the drug also increased the severity of the problem (1998a; 1998b).

Blood clots

Perhaps the most serious short term side effect of tamoxifen is the risk of developing blood clots (Saltman, 1994: 8). Thromboembolic disease has been reported to be up to seven times more common in tamoxifen treated patients, and in an earlier NASBP trial there were two deaths from thromboembolisms among women treated with tamoxifen while none occurred in the control group (Fugh-Berman & Epstein, 1992: 1144). At the early conclusion of the North American trial researchers were claiming that the rate of blood clots forming in the lungs rose from 9 to over 25 in every 10000 women (Gibbs, 1998: 15). While proponents of the trial argue this increase is inconsequential compared to the risk of breast cancer, the tamoxifen-related death count among trial participants tells another

story. Sharon Batt reports that five women died from breast cancer in the placebo group while six died in the intervention group; three from breast cancer and three from blood clots in the lung (Batt, 1998: 3). In light of these data, it appears that the benefits of tamoxifen may be seriously eroded by its side-effects and the success claimed by trial proponents may be premature.

Weighing up the effects

All of the conditions reviewed so far are effects of tamoxifen. The relative values which should be attributed to each of these conditions, how they should be monitored and how they should affect entrance criteria were fiercely contested between 1991 and 1994 as the trials were being established and practical aspects of their operation were being fine-tuned. The previous discussion has shown how the medical controversy (spearheaded by epidemiologists in the US National Women's Health Network) took the form of a methodological attack and a re-calculation of the risks and benefits of the US trial (which were far less optimistic than the trialists' predictions). This was accompanied by citing and counter-citing scientific articles published in reputable journals as a way of undermining the credibility of the assumptions made by those running the trials, and questioning the medical profession's ability to effectively monitor and treat the undesirable outcomes. Making claims about the ethical merits of the trial was another useful tactic. The National Women's Health Network had some limited success, forcing a congressional hearing into the trial in October 1992, and publicising the risks of endometrial cancer. But their lobbying did not stop the trial.

The way each of the above effects – whether intended or unintended – was weighted tells a story about the meaning of women's bodies and women's health to the advocates and opponents of the trials. For instance, low level, less serious side

effects were discussed, but were not counted in the risk / benefit ratios calculated by either group. These effects include nausea, early onset of menopause in premenopausal women, and exacerbation of menopausal symptoms such as hot flushes, depression, vaginal discharge, headaches, dizziness and irregular menses in postmenopausal women (Bush & Helzlsouer, 1993: 235; Oakley, 1991: 6). All these symptoms are associated with fluctuating hormone levels. The majority of attention has focused on the link between tamoxifen and life-threatening complications such as cancer and thrombosis. While these are significant, other side effects are more common, will affect more women, and are more likely to impact on quality of life and women's willingness to take up and maintain tamoxifen treatment. According to Ann Oakley, the most common complaint women make about their health is that doctors do not listen to them (Oakley, 1991: 6). Understanding how tamoxifen affects quality of life is just as important as understanding how it affects length of life. The fact that these symptoms are not even mentioned in the risk / benefit equations reflects the fact that trial organisers assumed they can be medically managed (by the prescription of anti-nausea tablets, HRT, analgesics, etc,) or simply ignored. But it also raises questions as to how seriously research clinicians will regard women's experiences of these symptoms, and suggests that the trialists may believe these maladies are a normal part of life for those living in the inherently pathological female body.

Paradoxically, the experience of precisely these symptoms could be responsible for the success or failure of the trials. Nicholson reports that when faced with an existing breast cancer, less severe side-effects contributed to about 5 per cent of women abandoning tamoxifen treatment for diagnosed breast cancer, and to 25 per cent of participants abandoning the pilot study which preceded the prevention trials (Nicholson, 1992: 1552). The figure of 25 per cent drop out suggests such

symptoms may have a major impact on the willingness of women to stay with the trials, and therefore on the outcomes of the trials. Indeed the Italian prevention study had to be stopped because of its drop out rate of 26 per cent (Batt, 1998). So it would seem participants do not regard these symptoms as normal or acceptable.

Informed consent

The positioning of 'less severe' side effects, and debate about side effects generally, raises the question of how informed consent is constructed within both experimental and routine medicine. Writing before the reissuing of UK consent forms, Carolyn Faulder (a member of the British Medical Research Council review committee) claimed that the information and consent form being offered to women entering the Marsden pilot trial was "a travesty of what seeking informed consent should be about" (Faulder, 1992: 32). The form mentioned only two side effects (mild nausea and headaches) and omitted both the more common hormonally-related side effects and the risk of endometrial cancer and eye problems outlined above. It did not mention a woman's right to withdraw from the trial at any time and concluded with the caveat "having fully explained to you the risks of participating in the trial, I must emphasise that the decision whether to participate must be entirely yours" (Faulder, 1992: 32). A draft consent form for the UK BCPT was presented to the MRC in November 1991, and while it was an improvement on the form used in the pilot, the organisers were still asked to produce a new, more explicit version. Faulder commented that her personal criticisms of the trial consent form "may seem trivial but [I] suspect quite a number of women might share [my] personal distaste for serious information being presented in first reader style and decorated with flowers in the manner of a tampon leaflet" (Faulder, 1992: 32).

Also discussing the trials before they commenced, Ann Oakley wrote that if "women in the tamoxifen trial are clearly informed about the possibility of such symptoms as hot flushes, headaches, depression [and] dizziness..., then they may be better informed than those who are being prescribed it outside a trial." She cited a survey by a British cancer support group of women with breast cancer being treated with either tamoxifen or another drug, 75 per cent of whom said they had been given no information about side effects (Oakley, 1991: 6). In Australia as in the USA, individual research centres are responsible for drawing up consent forms. During the 1992 US congressional hearing which took place after the trial had begun recruitment, 268 different consent forms were reviewed and more than two thirds required alteration (Ms., 1994: 21, editorial).

Even proponents of a tamoxifen prevention trial have reservations about the execution of the BCPTs. Dr Richard Love, American Cancer Society professor of clinical oncology at the University of Wisconsin, believed that a tamoxifen prevention trial should go ahead, but he argued that it should be more cautiously designed than the BCPTs. Love's own proposed prevention trial, rejected by funding agencies in favour of the NASBP trial, called for a pilot study involving 2000 postmenopausal women before a major trial, limited to women over 60, got underway. He felt the BCPT's design pre-empted many unresolved issues which need to be properly investigated but that Bernard Fisher, the NASBP director, was opposed to delaying the trial or launching subsidiary studies. In his opinion the trials treat women as "chattel" and represent "a dangerous trend towards medicalising prevention" (cited in Laurence & Weinhouse, 1994: 123-24).

According to critics, one of the points on which the trial organisers should have been more cautious was the inclusion of premenopausal women (Fugh-Berman &

Epstein, 1992: 1143-44). The published data available before the trials began suggested that tamoxifen is beneficial to postmenopausal women but the only evidence that premenopausal women might also benefit comes from an NASBP study whose results had not yet been published or subjected to the peer review that publication in a reputable journal supposedly elicits. And when the NASBP study was made available for scrutiny critics argued it should not be extrapolated to the tamoxifen prevention trials because of technical differences in the study populations (women in the NASBP trial were excluded if they had an oestrogen-receptor-negative tumour, while no such exclusions could be made in the prevention trials). When a premenopausal woman develops breast cancer she stands a greater chance than a postmenopausal woman that it will be receptor-negative, and these types of tumours are more frequently resistant to tamoxifen than are receptor-positive tumours (Fugh-Berman & Epstein, 1992: 1143-44). While the clinical evidence stacks up in favour of tamoxifen for some types of breast cancers in women over 50, in women under fifty the data are unclear. Roughly 20 per cent of breast cancers occur in women under 50 and in this group tamoxifen "is still just a research thing" (Richard Peto, quoted in Raloff, 1992: 266). At the start of the trials there were no clear data indicating the benefits of tamoxifen treatment in younger women, but proponents of the trials clearly believed it would have the favourable effects observed in older women. For example, when asked to speculate about the effect of tamoxifen in women under 50, Peto, director of the cancer studies unit at Oxford University, responded that he "suspect[s] the answer will be much the same as in older women" (cited in Raloff, 1992: 266). The fact that the trials were open to women aged 35 and over highlights again its scientific fragility: if the rationale for the trials is tenuous in the first instance (as its critics would have us believe), it is even more tenuous when it

comes to the inclusion of younger women. If the trials are deemed an unequivocal success they will help reconstitute tamoxifen as efficacious in treating younger women, but if results are more ambiguous, then adjusting the statistical analysis to exclude younger women will be one strategy open to those wishing to protect their perceived validity.

Younger women have at once more to lose and more to gain depending on the outcome of the trials. Assuming the drug does prevent breast cancer in some women, women whose cancers are prevented in their thirties or forties will theoretically benefit from a greater increased life expectancy than will women whose cancers are prevented in their sixties or seventies. Younger women will, however, also suffer the potential hazards of tamoxifen and the ongoing medical surveillance associated with its use for longer than their more elderly counterparts. Further, they stand to bear a greater financial burden. The estimated annual cost of the drug alone is between 600 (Butler, 1997: 304) and 700 [Glasziou P, 1994 #521: 10] Australian dollars. Ignoring inflation, the cost for five years (the equivalent of the trial) is between A $3000 and A $3500 per individual, and this amount does not include the price of subsidiary interventions which are likely to result from the treatment, such as endometrial biopsy. During the trial the drug was supplied free of charge to participants. In the UK and Australia it is possible that prophylactic tamoxifen may eventually be listed on the pharmaceutical benefits schedule. In the meantime, however, those wishing to continue treatment after the closure of the trials will bear the expense themselves.

Pregnancy – perpetuating neglect?

Finally, pregnancy is contra-indicated when using tamoxifen, and pregnancy or intention to become pregnant is grounds for exclusion from the trial (Bush &

Helzlsouer, 1993: 235). In Chapter 2, I discussed some of the issues surrounding the involvement of women in clinical trials and the potential problems associated with becoming pregnant while participating in such a trial. These issues are mirrored in the BCPTs through concern about the extent to which the trialists can control whether women become pregnant while on the trial and the effect of tamoxifen on children exposed *in utero*. In a letter to the *Lancet,* Goodare comments on a report that among the 85 women known to become pregnant while taking tamoxifen no foetal abnormalities have been detected. Rather than using this figure to indicate that taking tamoxifen during pregnancy is safe, she argues it indicates women will continue to become pregnant while taking the drug, despite official warnings. Goodare cites diethylstilboestrol (DES), once used to prevent morning sickness, and now linked with vaginal and testicular pathologies in those exposed before birth, as an example of a drug which initially appeared benign. As with the harmful effects of DES, she concludes that "[i]t may be twenty years before such problems [with tamoxifen] come to light" (Goodare, 1993: 444).

Despite this, the exclusion of potentially pregnant women highlights a concern which is central to the status of women in medicine generally and in clinical trials in particular: the assumption that women's bodies and social agency are intimately and unavoidably tied to their reproductive capacity while men exist unhampered by their reproductive abilities. Consider the implications of systematically excluding pregnant women from the tamoxifen trial. If the possible outcomes of the trial include a more widespread use of the drug in the community (which they surely must) then is it unrealistic to assume that no women in this group will become pregnant. Testing drugs in pregnant women is an extremely sensitive and difficult task which requires balancing the potential risks and benefits to the woman with maintaining maximum protection of the foetus. Recognising and

respecting a woman's autonomy and right to make decisions about her body during pregnancy has not been a feature of the history of clinical trials. In addition, ensuring the safety of drugs used by pregnant women requires long-term and systematic follow up, something which usually appears to be beyond the financial and practical capacity (and often the interests) of a research community increasingly motivated by a 'publish or perish' mentality. The sensitivities of involving pregnant women in clinical trials has resulted in the paradox that pregnant women who require medical treatment are likely to be exposed to drugs and procedures which have not been adequately tested (Merkatz et al., 1993: 295). Although I am not advocating testing tamoxifen on pregnant women, their exclusion from the trial population perpetuates the problems I have just outlined. In addition, no parallel exclusion clauses exist for men participating in trials who plan to or may impregnate women. This double standard not only implies that men are less intimately involved in the process of reproduction, but also points to the assumption that experimental drugs are less likely to affect the integrity of sperm than of an ovum or foetus. In this way male reproductive capacity is constituted as largely irrelevant to the workings of scientific medicine as opposed to female reproductive capacity which continues to be treated as a problem and used to justify exclusionary practices at all levels of medicine.

The 'gold standard' revisited?

Once the trials got underway, public debate over tamoxifen for prevention more or less subsided, and for about six years it was business as usual for the trialists (with the exception of new UK consent form in 1994). In April 1998, controversy erupted again when the North American trial was stopped early because trialists believed that tamoxifen was proving so successful that it was no longer ethical to

withhold it from women in the placebo group. Findings were leaked to the press before they could be peer-reviewed, causing intense world-wide media attention (Ault & Bradbury, 1998: 1107; Batt, 1998; Baum, 1998). After an average of 4 years on tamoxifen, 85 of the women in the North American treatment group had developed breast cancer compared with 154 women in the placebo group. This represented a substantial reduction. But while one disease had been prevented others had been induced. Women who took tamoxifen had significantly more cases of three potentially fatal conditions: endometrial cancer (33 in the experimental group vs. 14 in the placebo group), pulmonary embolisms (17 vs. 6) (Ault & Bradbury, 1998: 1107), and deep vein thrombosis (30 vs. 19) (Smigel, 1998: 647). In addition, more cataracts occurred among tamoxifen users (574 vs. 507) (1998b). Tallying the total death rate was also problematic: five women in the placebo group had died (of breast cancer), while six from the treatment group had died (3 from breast cancer and 3 from blood clots) (Batt, 1998). Claims about the cardiovascular benefits of tamoxifen also came to nothing with no difference being reported in the number of heart attacks between the two groups (Smigel, 1998: 648).

When the trial was halted, it was unblinded so women in the control group could be given the opportunity to take tamoxifen. The trialists also encouraged participants to enrol in a new prevention trial in which tamoxifen is being tested against another hormone drug, raloxifene. Although declared an unequivocal success by the trialists, the North American tamoxifen trial has not generated definitive solutions to the question of breast cancer prevention, so more scientific research must still be done but it will be difficult to conduct in the wake of the BCPTs. Instead, in the new RCT, tamoxifen, with all its uncertainties and unanswered questions, will be stabilised as the 'control' treatment against which

the unknown effects of raloxifene will be compared. The new trial will also be a large multi-centre study and despite problems of achieving the initial target of 16000 subjects for the NASBP prevention trial, organisers are confident of recruiting 22000 women (Gibbs, 1998: 15).

The unexpected early conclusion of the North American trial not only took other international tamoxifen researchers by surprise, but has led to their public condemnation of the conduct of American colleagues (Ault & Bradbury, 1998: 1107). The separate trials, although autonomous, were very much part of an international collaboration and the combined subject numbers and time-frame originally agreed upon were considered to be the minimum necessary to gather reliable data. Michael Baum, Professor of Surgery at University College London, describes the manner in which the findings were released as a 'subversion of the scientific process' and claims that:

> [t]he raw data, although interesting and encouraging, was associated with so much hyperbole and jingoism it would have been almost impossible for the uninformed lay public to avoid over-reaction, and it is highly likely that many frightened women with a familial predisposition to breast cancer are now demanding prescription of tamoxifen... (Baum, 1998: 8).

As the North American trial has been unblinded and results confounded by the invitation of subjects to participate in the tamoxifen vs. raloxifene trial, its outcomes cannot now contribute to any picture of the long term beneficial or detrimental effects of the drug. British researchers suggest that fifteen years of follow-up would be necessary to detect whether tamoxifen has a genuine preventive effect and the viability of this follow-up may now be in jeopardy as participants, hearing about American findings, may withdraw from other trials and

seek tamoxifen prescriptions. "If this should happen world-wide" writes Baum, "then 20 years of research development for the prevention of breast cancer mortality might come to nothing." (Baum, 1998: 7). Preliminary results from the IBIS trial suggest no reduction in the incidence of breast cancer, or at least a more modest reduction, (Pritchard, 1998:80) and researchers, in consultation with consumer advocacy groups, have decided to keep to the original protocol in the belief that it will provide the only reliable data on the ultimate worth of tamoxifen prevention (Ault & Bradbury, 1998: 1107; Baum, 1998: 7; Pritchard, 1998: 81).

Attempting to find an explanation for what he believes to be the scientifically untenable actions of his American and Canadian colleagues, Michael Baum looks to cultural factors, describing the litigious and commercial pressures facing American medicine as contributing to the early closure of the trial. He believes that fear of litigation, rather than a confidence in the authenticity of tamoxifen's apparent preventative actions may have prompted the release of findings once significant differences started to appear between the two groups:

> One can easily imagine what might happen in five years time if a woman on the placebo arm developed breast cancer and it was discovered that the clinical trialists knew that tamoxifen prevented cancer many years earlier (Baum, 1998: 7).

In addition, he points out that the patent on tamoxifen has run out in Europe and does not have long to go in the USA, suggesting that a speedy release of positive findings may be the most profitable way for ICI Pharmaceuticals and its stock holders to benefit from the trial (Baum, 1998: 7). In Baum's account there is no scientifically explicable reason for the early closure of the trial. Instead, he uses sociological explanations to account for the corruption of the scientific process. In

this way the 'gold standard' of scientific evidence-based medicine remains untarnished.

Contesting claims and replication

In Chapter 1 I discussed the belief that scientific knowledge can be codified into a set of unambiguous instructions which can be transferred between scientists and applied in order to reproduce the results of another's experiment (see Collins, 1982). I also discussed the role of 'replication' in the confirmation of scientific findings, and argued that 'replication' has a different meaning for an RCT than it does for more laboratory-oriented science. Like the tamoxifen prevention trials, many RCTs are large population-based interventions where 'replication' is both duplication of the effects of a drug or procedure at an individual level, and the production of the statistical likelihood with which a treatment effect can be generalised to broader populations. Treatment in every patient represents a mini-replication, in terms of the effects of tamoxifen in a specific subject, and collectively these contribute to the replicability of the trial as a whole. In the case of the BCPTs, the duplication of the trial in different centres and in different countries also constitutes a form of scientific replication.

This chapter has shown that medical researchers have numerous strategies through which they can question the accuracy of clinical studies. Strategies which involve contesting technical details or making claims about methodological rigour, will be underdetermined by assumptions about the role of replication in science. For example the critics of the BCPTs can argue that replication will not be valid by claiming the trialists have not adequately represented the effects of the drug within individual women nor accounted for unspecified side effects in the monitoring protocol. Disagreeing with the definition of appropriate subjects for the trial and

consequently the relevance of the outcomes for broader populations of 'high risk' women is another way of problematising replication. These criticisms identify problems with ensuring replication of the actions of the drug in individual women. Further complications arise in light of the fact that the trials are carried out in numerous locations in multiple centres, all of which highlight the potential problems of ensuring the consistency of physician practices, treatment procedures, and monitoring throughout the different trial sites. From the perspective of a sociology of medical knowledge, the question of replicability within different centres has not been problematised except through the issue of ensuring quality control. This is, no doubt, largely because the multi-centre trial is an accepted institution within medical research, and is based on the premise that the rules of experimental procedure can be transferred without the loss of information. To question the effect of multiple study sites on the outcomes of the trials would raise deeper methodological questions about medical research practices (for example, see Timmermans & Berg, 1997). Finally, the current disagreement between the IBIS and the NASBP trial organisers over the early termination and the usefulness of continuing the remaining trials disrupted the replication of the trial across national boundaries.

Conclusion

It is clear that there are no easy answers to the problem of breast cancer prevention, and tamoxifen may provide a partial solution. But what does this mean for the current prevention trials and the heated controversy they have provoked?

The authority attached to different types of written accounts can become central to the interaction between participants within scientific debates. In particular, the extent to which various critiques and commentaries appeal to a scientific

grounding in establishing their claims or negating the claims of their opponents demonstrates the high esteem with which objective knowledge is regarded and its status as a tool for legitimation. Mapping specific controversies in the establishment and execution of the trials shows that even within debates about technical aspects of the trials operation or assessment, those debates have not been dependent upon disembodied scientific standards. Despite this, the rhetoric of adherence to such standards, coupled with deference to empirical data - the symbolic materialisations of those standards - has been a feature of the medical controversy. Further, the professional interests of the trialists have resulted in a specific constitution of prevention in the trials. 'Prevention' has become an entity which should be administered by biomedical specialists, without regard for economic, social or political concerns, and something in which nutritionists, public health experts and most especially, women's health experts, should have minimal input. In addition it is constituted as something in which the profit motive plays a part.

CHAPTER 6

Hormones, Masculinity and Men's Health

The previous chapters have argued that social values are naturalised and become incorporated into the practices of medicine and the human body through the RCT: the actions and effects of female sex hormones have been produced as a natural constituent of certain types of femininity, and assumptions about the relationship between the female body, sex hormones and sexual identity this entails were incorporated into the tamoxifen prevention trials. This chapter shows that similar dynamics are also at work in the construction of masculinity through discursive practices involving male hormones and cancer medicine, although the genders reified through male hormones are quite different from those at work in the construction of femininity. Examining prostate cancer as an example of a sex-specific disease which is currently represented as dependent on male sex hormones provides a good parallel case study for my work on breast cancer because:

1) prostate cancer is an exclusively male disease, like breast cancer's construction as a women's disease;

2) hormones dominate representations of the causes of and risk factors for prostate cancer as they do breast cancer;

3) prostate cancer is a high profile issue around which advocates of men's health have organised in much the same way that breast cancer has been the focus of activism by the women's health movement;

4) the effectiveness of screening and detection technologies is controversial and, as with breast cancer, these ambiguities highlight the way technologies, beliefs and practices are constituted in relation to one another;

5) the research agenda is predominantly controlled by and serves a similar range of professional interests to those served by breast cancer research (orthodox cancer specialists at the expense of allied health workers addressing issues such as the link between diet, lifestyle and environmental exposures and prostate cancer); and finally,

6) a hormone-based prostate cancer prevention trial is currently underway.

Men's health and gender

While questions about the gendered nature of power have been well rehearsed, to date the majority of thinking about gender and health has been fostered by the women's health movement and feminist scholarship (Sabo & Gordon, 1995: 3), and reflects a feminist orientation (Connell, 1992: 736). Consequently, when 'gender' is flagged as a health issue there has been a tendency to assume both that one is talking about women's health and that men are ungendered or that the construction of masculinity is unproblematically beneficial for men. Since the mid 1980s, however, debates about gender have broadened and a men's critique of gender has emerged. This shifting terrain of gender studies has facilitated a recognition of the special health needs of men. Apart from sex-specific conditions, such as testicular and prostate cancer, statistical data on morbidity and mortality rates for conditions affecting the whole population consistently reveal that being male is a health risk. This risk is evident across a wide spectrum of life events; males have a higher perinatal and early childhood death rate, suffer more

congenital birth defects, have a greater likelihood of experiencing recessive sex-linked disorders, are more prone to be injured intentionally or as a result of an accident, and have a higher incidence of behavioural and learning disorders than females (Harrison et al., 1992: 271). The age-specific death rate for men and adolescent boys is also higher than for women and adolescent girls: young men are more likely than young women to die from accidents, suicides and drug dependency, while older men die from heart disease and many common cancers at higher rates than older women (Fletcher, 1996).

In order to understand the poor health status of men and boys in our community a number of issues must be considered. These include questions about the health effects of biological differences between the sexes, the availability and quality of health services directed towards the needs of men and boys, and the relationship between patterns of socialisation and gender identity and well-being. Throughout this thesis I have argued that any knowledge of biological sex is available only because of the cultural and historical production of certain kinds of bodies and gendered subjectivities. Because of this it is crucially important not to assume that the statistics on men's pathologies speak for themselves. Instead they should be viewed as a product of the broader social climate which influences the provision of health services and the lived experience of those pathologies. For example, most Australian men have access to quality basic medical care but some evidence indicates they are less prepared than women to use it (Lawrence, 1995: 7). Why should this be the case? The effects of current constructions of masculinity provide a partial answer.

The notion of hegemonic masculinity remains important for discussions of men's health as it provides a reference for articulating a culturally honoured or desired set

of gender traits for men against which the multiplicity and fluidity of contemporary masculinities can be contrasted. According to Connell, examining the diversity of men's experience of gender and the ways these are enacted in daily life often identifies contradictions in men's desires and behaviour. The tensions between perceived gender identity and the enactment of that identity provide a point for identifying changing expectations about gender (Connell, 1997: 15). As such, they can also provide a point at which to direct strategic health interventions. For example, consider the health implications of the following descriptions of masculinity. Harrison et al., claim that traditional western masculinity encourages men to be "non-communicative, competitive and non-giving, and inexpressive, and to evaluate life success in terms of external achievements rather than personal and interpersonal fulfilment" (Harrison et al., 1992: 272). Connell stresses the importance of images of masculinity in the formation of an Anglo-Australian identity: images which posit the masculine as self-sufficient, egalitarian, rough-and-ready man's man of the Anzac legend (Connell, 1997: 15). The enactment of such masculinities translates into a tendency for men not to seek medical help when they are ill (Buchbinder, 1996: 41). Michael Kimmel writes that "'Real men' don't get sick, and when they do, as we all do, real men don't complain about it, and they don't seek help until the entire system begins to shut down" (Kimmel, 1995: vii-viii). Health is an area in which the hazardous effects of hegemonic masculinity are clearly evident, so addressing the problems of men's health requires an investigation of, and possibly a challenge to, the way men participate in contemporary masculinities. The high rate at which young men are involved in road accidents is a case in point. When young men engage in dangerous driving, such as speeding or driving when drunk, they are preforming a specific form of gender practice. According to Connell:

> They are acting that way in order to be masculine. The dangerous driving is a resource for their making of masculinity. Here the active construction of masculinity is a key to the risk-taking behaviour, and to strategies of prevention (Connell, 1997: 17).

That risk-taking by young male drivers is a means of producing masculinity is suggestive of the multiple gender positions available to men and the way these are embedded within the social and historical worlds. Young western men may utilise the resource of risky driving because of peer group identification with a globalised 'car culture' (Connell, 1997: 17). But the symbolic meanings attached to the car vary geographically, historically and throughout an individual's life. In communities where access is limited, or among middle aged or elderly men, the car may not assist the preformance of masculinity, or may warrant the preformance of a different masculinity. Since men are not an undifferentiated group with equal access to social and personal power, they experience the exercise of social power, including patriarchal domination, differently (Connell, 1992: 736; Sabo & Gordon, 1995: 12-13). So road safety campaigns will theoretically be most successful if they account for this diversity and use it to moderate risk-taking behaviours among men with a range of social identities. Changing the way young men drive is, therefore, no small task as it actually involves refiguring gender identity. According to Sabo and Gordon:

> Men's roles, routines, and relations with others are fixed in the larger historical and structural relations that constitute the gender order. Critical feminist perspectives remind us that any realistic agenda for the transformation of the self and gender relations has got to go beyond

> therapeutic visions and practices... without changing the political, individual [change] will erode and fade away (Sabo & Gordon, 1995: 16-17).

As with early struggles to define and understand 'women's health', developing an appreciation of the relationship between contemporary masculinities and health, will need to be accompanied by a more specific investigation of the types of masculinity assumed within orthodox medicine and the way medical discourse reinforces and reinvents those masculinities. In particular, how have representations of the vulnerability of male bodies to disease influenced the expectation of individual patients and practitioners (both male and female), the intention and type of research being carried out, and policy decisions and the provision of services? Further, how have these medical discourses been expressed within the social sciences and epidemiology, and how do they account for specific factors which are seen to bring about men's apparently poorer health status? What factors in social life might contribute towards or alleviate men's health problems or our understanding of them? In much the same way that discourses about female sex hormones provide a tool for understanding women's health, so too can the multiple representations of male sex hormones provide a focus through which the questions above can be addressed.

Feminist critiques of health which focus on the effects of gender on women's health status can provide a starting point for investigating the impact of masculinity on men's health, and indeed, such approaches seem to have been widely adopted. Writing within men's studies, Donald Sabo and David Gordon state:

> We owe our intellectual origins to the sociocultural model in mainline social science, feminist theory and research, and the incipient efforts of feminist-identified men to rethink men's health issues (Sabo & Gordon, 1995: 4).

Further they argue that their work contributes towards the development of an "'inclusive feminism' that facilitates systematic study of men and masculinity" (Sabo & Gordon, 1995: 4). As well as theorising the frailty of the human body, feminist scholarship has engaged productively with certain constructions of femininity, bringing about a social movement to improve women's health. In order to achieve similar goals, theorists working in men's health have attempted to modify feminist theory and practice to account for the different relations of privilege and power among men (Sabo & Gordon, 1995: 12-13).

It is, on the whole, a positive development that the theoretical and methodological insights of feminism are sufficiently nuanced to be able to contribute toward understanding the diverse health experiences of men. Nevertheless, the appropriation of feminist perspectives by men's health scholars poses some problems. Critical feminism is built on the premise that social inequities profoundly inform the lived experience of gender. Unless explicitly drawn out, these inequities can appear to be naturally occurring. Feminist concerns about women's health centre on the belief that biomedicine is male-centred in both its epistemological foundations and its material operations. In light of the centrality of the assumption that medicine privileges men, the application of feminist thinking to developing an agenda for men's health appears problematic. If, as feminist theories of health argue, both the beliefs and practices of medicine are inherently male oriented and it is the task of feminism to reveal and redress this orientation,

how can feminism hope to offer any insights into men's special health needs? And should not, according to this premise, those needs already be catered for?

The claims that masculinity and male sexuality are socially constructed rather than biologically determined in the strict sense, are a constituent part of feminist theories about the social complexities of sex. Despite this, examination of the specific differences between men and the situations and social parameters within which they exercise or experience dominance raise particular issues about the ways gendered power is linked to other forms of authority (Ramazanoglu, 1992: 339). It is now becoming apparent that men and boys are inadequately served by a medical system that does not acknowledge the relevance of male gender identity to health. At the same time, however, the androcentrism of medicine has resulted in research, funding and treatment regimes which advantage males (Fletcher, 1996: footnote 14). Areas which need not be specifically sexed yet continue to have a distinct male bias include the provision of services such as veterans hospitals and occupational health programmes, and specialties such as cardiology, sports medicine (Connell, 1997: 14). Urology is another example.

Masculinity continues to symbolise social power. Feminism has used a righteous anger against male oppression of women to organise women into demanding social equity. The study of masculinity, however, has too often been fuelled by the guilt men feel when recognising the illegitimacy of women's continued social subordination or by a defensive anti-feminism (Ramazanoglu, 1992: 339; Tacey, 1997: 23). In light of this, men who resist hegemonic masculinity are undertaking a distinctly different activity from women who resist femininity. Adopting the approach taken by Nancy Hartsock (Hartsock, 1990), Ramazanoglu describes the

critical study of masculinity as being similar to the concept of the coloniser who resists the process of colonising:

> He will not behave like other colonisers, but he cannot become one of the colonised. In a comparable argument, men who resist masculine dominance cannot become women, they become failed men and betrayers of masculinity... [T]his form of resistance makes political activity difficult because there is no basis for mass support. The possibilities for change may then be seen as lying at the level of men's personal growth, emotional freedom, and restructured relationships (Ramazanoglu, 1992: 347).

But finding themselves in conflict with dominant masculinities need not leave men who engage with the gender order disenfranchised. Moves within poststructuralism and postmodernism have allowed current feminist critiques of health to acknowledge that the exercise of power is highly fluid and gender is not simply imposed through structured forms of socialisation. Rather, individuals actively participate in the construction, reconstruction and maintenance of gendered power relations. Because it endeavours to account for the fluidity of particular cultural relationships of power, feminism does offer tools which can help understand masculinity and the multiple ways it affects health status. But as feminist empiricism and standpoint feminism show, men have never occupied the same political position as women. Nor do they share women's embodied experience of sex or gender. Scholars and activists who attempt to mobilise a men's health movement should not expect to fulfil the same function as the women's health movement or the feminist scholars and activists who continue to maintain a watch should the injustice and discrimination of the past resurface. To be useful for understanding men's health status, critical feminism must be used reflexively with

due consideration to its historical and political origins. With this caveat in mind, it is worth noting that an emphasis on the gendered nature of men's health encourages service providers and policy makers to take gender seriously as a health concern; a move which must surely benefit women's health. In addition, women's health also stands to benefit from the insights gained in the critical analysis of a men's health (Broom, 1994 404; Broom, 1998).

Masculinity and hormones

In Chapter 3 I discussed the construction of androgens as crucial for sexual differentiation of foetuses, the subsequent triggering of secondary sex characteristics in boys at puberty, and the differentiation of the brain structure, contributing to supposed gender differences in patterns of cognition and cognitive ability. I showed that the evidence offered to support each of these hypotheses has been coded and inscribed to reflect cultural assumptions about gender. A third crucial site at which masculinity, men's bodies and hormones intersect is in the construction of sexuality.

When considering the role hormones play in the development of masculinities, one immediately confronts the literature linking male biology with physical aggression and social dominance. Males, it would seem, be they laboratory rats (Kriegsfeld et al., 1997), adolescent criminals (Dabbs et al., 1991), or participants in chess tournaments (Mazur et al., 1992), are driven by their hormones to seek status through confrontation. According to authors such as Barash and Goldberg, this desire for competition and conquest is as a result of their hormones, the male birthright. Should women acquire these qualities it will never be to the same extent as men, in whom such characteristics are naturally predetermined (Barash, 1979; Goldberg, 1993).

When it comes to relations between the sexes, the male tendency toward aggression and competition can take the form of male sexual domination of women. The role of male sexuality in perpetuating male power came under intense scrutiny by feminists during the 1970s and the early 1980s when it became viewed as fundamentally linked to male dominance. Authors such as MacKinnon, Dworkin, Morgan, Griffin and others, argued that male sexual dominance was central to all other power relations in society (see Segal, 1990, second edition 1997: 207-8). It was not just feminists, however, who have viewed the 'phallic imperative' as an organising social force. According to Steven Goldberg;

> There is an enormous amount of evidence which demonstrates beyond doubt that the testicularly-generated foetal hormonalization of the male central nervous system promotes earlier and more extensive maturation of the brain structures that mediate between male hormones and dominance behaviour; this makes the male hypersensitive to the presence later on of the hormones which energise dominance emotions and behaviour, and result in his stronger tendency to respond to the environment with dominance behaviour (Goldberg, 1993: 79).

This tendency, argues sociobiologist David Barash, results in a wide range of behaviours, including a propensity towards social dominance and a tendency towards criminal activity. These can be manifest in behaviours such as reckless driving, lynchings, modern warfare, and even genocide (Barash, 1979). A more recent, more modest and better researched version of this view can be found in the work of Theadore Kemper who argues that a 'socio-bio-social' feedback mechanism is responsible for the production of testosterone and its behavioural effects, which are manifest primarily through a tendency towards aggression and

dominance, or 'eminence-seeking behaviour' (Kemper, 1990). Despite the ambiguous scientific status of these works, Fausto-Sterling, a biologist who has extensively analysed gender bias in the biological sciences, believes the ideas they perpetuate are very alluring:

> [t]he idea that male hormones make men more competitive, better at sports, go-getters in the business world, and ready to fight to defend their honour and family certainly captures the popular imagination (Fausto-Sterling, 1985: 126).

But more than simply 'capturing the popular imagination', these discourses also express and replicate dominant cultural beliefs about sexuality. According to Segal the new 'scientific' study of sex that emerged in the mid-nineteenth century (a discourse in which hormones featured prominently) formalised depictions of masculine sexuality as a natural, overpowering and insatiable force (Segal, 1990, second edition 1997: 208). As discussed in Chapter 3, first male internal secretions then sex-hormones, were 'written in' to science's rendering of sex. This portrayal of male sexuality has continued throughout the twentieth century, producing males' need for sexual dominance and continual pursuit of procreative opportunities as seemingly self-evident truths (Segal, 1990, second edition 1997: 209). The dichotomies which permeate scientific writings about sex (dichotomies such as 'masculine / feminine', 'active / passive' and 'conquest / submission') contribute to the construction of heterosexual intercourse as the foremost moment of male domination and female submission, and as inevitable (Segal, 1990, second edition 1997: 209). In the current milieu the phallic status of the heterosexual male body pervades cultural representation of the male body (Waldby, 1996) and

performance, penetration and conquest are important forms of male symbolic capital (Cameron & Fraser, 1994).

While the phallus remains a site at which cultural and biological meanings converge, the nature and articulation of those meanings are highly contentious. This is particularly evident within medical discourses about prostate cancer because hormones are physiologically necessary to achieve an erect penis. Negotiating the boundaries between medicine, male bodies, masculinities and hormones highlights the fragility of the phallus and suggests a number of arenas in which its significance is being re-constituted. Male bodies are, therefore, a site at which knowledges and practices are changing, and possible embodied, technological and professional futures are being constituted.

The medical picture of prostate cancer

The prostate is a walnut sized gland located below a man's bladder and surrounding the upper end of the urethra. It is part of the reproductive system, necessary for the production of viable semen, and does not reach maturity until after puberty. In developed Western countries prostate cancer, the malignant enlargement of the gland, is the second most common cause of cancer deaths among men (after lung cancer), and the most common cause of specifically male cancer death (Smith et al., 1998: 3; Wasan & Waxman, 1992: 477).

Prostate cancer is said to be a disease with remarkably low virulence; the majority of men who develop prostate cancer will die *with* it rather than *of* it. It is unique among human tumours in that the number of confirmed invasive cancers found during autopsies exceeds the number of cases which are confirmed during life. In other words, death from 'other causes' is likely to occur before the clinical

symptoms of prostate cancer develop (Australian Health Technology Advisory Committee, 1996: 15). Autopsy studies have shown that more than 30 per cent of men over the age of 50 have evidence of incidental prostate cancer at death (Brawley et al., 1994).[8]

Like most solid tumour cancers, prostate cancer becomes more common as men age. It is relatively rare in men younger than 45 but the risk increases dramatically by the time a man reaches 60 years of age (Brawley et al., 1994). In 1994, 2590 Australian men died of prostate cancer. Over 62 per cent of these deaths occurred in men aged 75 years and over, and 41 per cent occurred in men aged 80 years and over (Australian Health Technology Advisory Committee, 1996: 5). Until the age of about 45-50 the size of the prostate stays fairly constant, however as men age the gland often becomes enlarged and can constrict the urethra causing blockage and pain while urinating. In most cases these enlargements are non-cancerous, a condition known as benign prostatic hyperplasia (BHP), which is thought to indicate an elevated risk of developing prostate cancer.

As with breast cancer, the incidence and mortality rates of prostate cancer have increased in the last two decades, although the incidence is increasing faster than mortality (Feigl et al., 1995: 161). There is speculation that the reported increase in incidence rates may be an artefact of greater medical surveillance and the proliferation of new diagnostic techniques (Australian Health Technology Advisory Committee, 1996: 17). Although improvements are being made to existing treatments, the past two decades has seen no substantial reductions in mortality rates.

---

[8] Despite this, in Australia the five year survival rates for men with clinically confirmed prostate cancer (78.9 per cent) is not substantially better than the five year survival rate for women with breast cancer (76.8 per cent) (Smith et al., 1998). However, it tends to occur at later ages.

In the past, prostate cancer was often diagnosed at an advanced stage after tumours had metastasised, but the development of prostate-specific antigen screening (PSA) is believed to have improved the detection of earlier stage malignancies. PSA testing came into use in the mid 1980s and has dramatically altered diagnosis and treatment options. Before the widespread use of PSA the only method for detecting tumours, digital rectal examination of the prostate (DRE) with follow-up needle biopsy, meant that tumours had to be large enough to feel through surgical gloves and the wall of the rectum, and therefore tended to be larger and more advanced than tumours which can now be detected using PSA and needle biopsy. Like mammography, the primary objective of PSA is early detection of tumours, and like mammography, developing acceptable, appropriate and reliable base lines of the specificity and sensitivity for diagnosis has proven to be difficult.

The full impact and worth of PSA testing is yet to be clarified, however one outcome is that treatment may be 'moved forward' relative to the age and stage of tumour development. While this opens up new opportunities for researching the effectiveness of treatments and the natural history of the disease (Grove, 1996: 37), it also changes medical and broader community perceptions of prostate cancer, masculinity and men's bodies. The writings of Margrit Shildrick provide a means of articulating some of these changes. In her work *Leaky Bodies and Boundaries,* Shildrick draws attention to a strategy used by lobbyists from the disabled community who encourage the 'healthy' majority to recognise they are "merely temporarily able bodies" (Shildrick, 1997: 60). While the lobbyists intended to do no more than highlight the indeterminacy of the physical body, Shildrick argues that the approach they used also accentuates the permeability of the boundaries between health and ill-health, and abled and disabled bodies. More precisely, it shows that:

> the regulatory and disciplinary regimes which impose and maintain normative standards of bodily and mental well-being are necessary precisely because of the inherent leakage and instability of categories, because the spectre the other always already lurks within the selfsame (Shildrick, 1997: 60).

The adoption of screening technologies such as PSA at once draws attention to the delicacy of the male body while also invoking normative standards of male embodiment which largely disavow the possibility of physiological or psychological frailty. Previously understood as a disease of older men, the possibility of prostate cancer now looms over men at ever earlier ages. While prostate tumours are not always life threatening, the side effects of treatment, which include incontinence and impotence, can be severe. In addition to the physical consequences, a diagnosis of elevated serum levels or prostate cancer will result in a man confronting and often transgressing a number of elements central to contemporary masculinities. A diagnosis will focus an individual's attention on the degeneration of his body; an early diagnosis means this happens at a younger age. It will propel a man into a relationship with the medical profession through his perceived need for more testing, monitoring and possibly treatment. It can also constitute the boundaries of younger or middle aged bodies as permeable, as they are performed upon by those involved in the medical diagnosis, treatment and surveillance. And individuals may find their bodies leaking and have their sexuality compromised as they live with the consequences of being responsible medicalised subjects.

Along with this leakage of the corporeal body comes a leakage from the category 'male'. Within modernity it is 'woman' whose borders are thought to be permeable

both physically and as rational subjects (Shildrick, 1997). Men are constituted as more stable and self-contained while women lack containment, being instead indeterminate 'other' occupying an ambiguous boundary position where nature and culture flow into each other (Grosz, 1994; Ortner, 1974). According to Ortner, women's role in 'species life' and the physicality this entails, is one factor which may have contributed to the culturally constructed conviction that women are closer to nature than men (Ortner, 1974). Because of this physicality the female body cannot be discreetly contained, instead the inside leaks out (during menstruation, birth and lactation), and the outside or 'other' enters within (during heterosexual intercourse and pregnancy). With the flows to and from the female body comes the possibility of physical and symbolic pollution or contagion as the boundaries of the subject are transversed (Douglas, 1984; Ortner, 1974: 70-72). In contrast, the idealised phallic (heterosexual) male body serves as a prophylactic against the types of contamination to which the bodies of women and gay men are subject (Waldby, 1996). This phallic body is an immunologically perfect body without orifices, impenetrable both physically and as a symbolic representation of a cultural ideal. And this idealised heterosexual male body is only possible because of a disavowal of receptivity in dominant configurations of masculinity which displaces anal and oral receptivity and passivity onto women and gay men (Waldby, 1996: 13-14). The incontinent, impotent, man who is subjected to the medical penetration of his orifices may find himself unceremoniously called into an intense relationship with his corporeal body. In so doing he deviates from the normative standards of 'maleness', and takes up an embodied subjectivity traditionally occupied by women and (at least since the emergence of AIDS) gay men.

Understanding and constructing prostate cancer risk

At the moment there is no technique equivalent to the Gail model (discussed in Chapter 4), which can be used to calculate an individual's risk of prostate cancer, and researchers consider developing such a model to be a priority (Feigl et al., 1995: 161). 'High risk' groups are, however, generalised as being those with a strong family history of prostate cancer, African and Afro-American men, or men with certain types of benign prostatic abnormalities. The factors which identify these risk groups are not adequately understood but, analogous with breast cancer, are represented as being hormonally and genetically based. Family history refers to a genetic link (and may indicate a tendency towards hormonal risk), being black refers to the racial differences in the production of testosterone, and benign prostatic abnormalities may be a precursor to malignant disease and result from either of these sources. There is a reported ninefold increase in the odds ratio observed in men who have first degree relatives with prostate cancer. Genetic prostate cancer appears to affect younger men, with reports indicating that 43 per cent of men with prostate cancer diagnosed before the age of 55 years have relatives with the disease (Brawer & Ellis, 1995: footnote 21; Giovannucci, 1995: 1772). A prostate cancer-specific gene has not been identified although research attempting to identify one continues. More controversial indicators of elevated risk include diet, geographical location of the population in question, vitamin D deficiency, and whether a man has had a vasectomy. But in general, risk factors remain hazy and imprecise and follow the trends of risk categories associated with the breast cancer and other solid tumour cancers. Brawer & Ellis write that "[e]ven with the identification of these high-risk groups, given the incidence of prostate cancer, ultimately all men constitute the potential population for prostate cancer prevention protocols" (Brawer & Ellis, 1995: 1784).

Racial and ethnic variation in prostate cancer rates are considered important for understanding the disease. Previously, autopsy information indicated that rates of indolent prostate cancer in Afro-American and white American men were similar, despite racial differences in symptomatic prostate cancer. This finding led researchers to assume that serum testosterone levels (reported to be 15 per cent higher in black men compared with white men), were responsible for the increased incidence of prostate cancer among black men (Ross et al., 1976). More recent research indicates that African and Japanese are less likely than American men, to develop clinically significant prostate cancer (Brawley et al., 1994). Because of their increased risk compared to white American men, Afro-American men are a particular target group for both screening programs and prevention trials.

When cancer researchers treat racial and ethnic variations as significant, they tend to reify assumptions about the essential difference these categories entail. For example, in their study of the hormonal basis of variation in prostate cancer rates, Ross et al., give a detailed breakdown of rates among African Americans, whites (either Latino or non-Latino) and Japanese and Chinese Americans. They write:

> We long have believed that understanding the racial-ethnic variation in risk was critical to achieving a general understanding of prostate cancer aetiology and of prevention strategies. There are compelling reasons to believe that androgens are involved intimately in prostate cancer development and in the racial-ethnic variation in risk (Ross et al., 1995: 1778-9).

In this instance racial and ethnic difference is a proxy for a quantifiable average biological difference. This study compared circulating testosterone levels in young men who the researchers identify as being in the same ethnic group with known rates of prostate cancer. They conclude that differences in the production of

prostatic 5-α-reductase could contribute to racial differences in prostate cancer rates (Ross et al., 1995: 1778-9). Such an explanation solidifies the boundaries which contain racial categories, reduces those categories to a question of dichotomous measurable biological difference (rather than considering the cultural aspects of ethnicity) and thereby naturalises them. Despite attempting to remove the question of racial variation in prostate cancer rates from social and cultural explanation, Ross and colleagues defer to the causative role of male sex hormones which (as this thesis has shown) invokes historically constituted discourses about the construction of male sexuality.

Major 'environmental risks' implicated in prostate cancer are dietary patterns and geographical location. Professional opinion is divided as to whether diet genuinely influences prostate cancer, however regional and cultural difference in diet might offer an explanation for national, and international variation in incidence. Some argue that the evidence supporting a link between diet and prostate cancer is "circumstantial at best" (Brawer & Ellis, 1995: 1784), while others believe that dietary factors "appear to hold the most promise for primary prevention" although they acknowledge that the precise factors and mechanisms must be better understood (Giovannucci, 1995: 1766). One hypothesis about a link between diet and prostate cancer is that the breakdown of dietary fat increases production of testosterone in men, thereby elevating risk (Hill et al., 1979). As with the breast cancer literature, this move constitutes 'environmental risk' as meaning 'personal biological environment' and erases reference to broader socially orchestrated exogenous environmental factors. Despite the lack of consensus, a correspondence between national per capita fat intake and prostate cancer incidence has been documented wherein the higher the fat intake the higher the national incidence of prostate cancer (Brawer & Ellis, 1995: 1784). According to Giovannucci, the

incidence rate of clinical prostate cancer varies substantially between countries. Although much of the 120-fold variation he refers to may be due to different national patterns of cancer detection and hence not 'real', it is clear that significant regional variations do exist (Giovannucci, 1995: 1766).

Finally, vitamin D exposure and whether a man has undergone a vasectomy have also been implicated as a risk factors. Rates of prostate cancer increase the further one travels from the equator and serum levels of vitamin D have been reported to be lower in men with prostate cancer than in the general population. Together this data suggests that exposure to natural sunlight and synthesis of vitamin D may be important. Giovannucci et al., have identified an apparent increase of relative risk of 1.56 in men who had a vasectomy (Giovannucci, 1995). However subsequent research has failed to confirm a clear association between vasectomy and prostate cancer (Brawer & Ellis, 1995).

With the exception of vitamin D deficiency and vasectomy each risk factor listed above makes reference to sex hormones. Since the late nineteenth century there has been speculation that malignant prostate cells can flourish and grow only in the presence of androgens (White, 1893). Although the precise role androgens play in causing prostate cancer remains unclear (Brawley et al., 1994: 595), the existence of a link is widely accepted, and standard treatment now involves implementing some form of androgen deprivation. While androgen deprivation eases the symptoms in up to 85 per cent of men it does not improve survival, and once prostate cancers have metastasised current treatments are not curative but aim instead for an improvement in quality and length of life (Wasan & Waxman, 1992: 477). Hormonal treatments do not focus solely on androgens; oestrogens were

introduced to prostate cancer regimes in the early 1940s and continue to have an ongoing role in treatment (Wasan & Waxman, 1992: 477).

As with breast cancer, prostate tumours may become hormone resistant after several years of treatment with hormonal drugs (Brawley et al., 1994: 596). Nonetheless, advocates of hormonal manipulation argue hormones may be an effective form of chemoprevention even if prostate cells become androgen insensitive following treatment. As the mechanism of tumour resistance is thought to follow principles of Mendelian genetic replication the patient may still benefit from a regression of their tumour even if androgen insensitive cells do survive the process of hormone treatment (Brawley et al., 1994: 596). Tumour regression does not necessarily correspond to increased life expectancy or a reduction in the virulence of the disease, but it may diminish symptoms. Current hormonal treatments are thought to show promise as preventive agents were it not for their negative impact on sexual functioning (Brawley et al., 1994: 596). The hormones which are said to be most dangerous to the prostate are testosterone and dihydrotestosterone (DHT).

Preventing prostate cancer

Because of the difficulties of treating later stage cancers, increasing attention is being directed toward early detection and prevention of prostate cancers (van der Meijden, 1999). While there are a number of possible strategies for the prevention of prostate cancer they have not yet been fully explored and, like the strategies for preventing breast cancer, researchers believe there are substantial practical problems associated with them. These include investigating the link between environmental toxins, various risk-taking behaviours, the administration of chemoprevention agents, and prostate cancer prevention (Brawer & Ellis, 1995:

1784). No clear cut environmental toxins have been identified, which rules out the first of these options. Other than being male, the risk categories for prostate cancer are not clearly defined, so modification of risk-taking behaviour is also impractical. A possible exception to this is the strategy of altering diet, but the cancer industry remains sceptical that large, long term trials based on behaviour modification are feasible. According to Brawer and Ellis:

> Problems with dietary modification include patient compliance, the probable need for long-term change, and the possibility that dietary changes must begin very early in life... [S]tudies to show the efficacy of such changes would require very large cohorts (Brawer & Ellis, 1995: 1784-85).

Because of these difficulties Brawer and Ellis believe such trials are not possible. It should be noted that the number of participants required by both the BCPT and the PCPT must be considered as 'very large cohorts'. As discussed in Chapter 4, the design and operation of dietary trials do not fall within the conventional professional domain of oncology and would need to be administered in conjunction with (if not exclusively by) primary health educators and nutritionists, epidemiologists and biostatisticians. As patterns of food consumption are presently the only identifiable 'risk-taking behaviour' open to manipulation, in the eyes of the cancer establishment the problems of administering behaviour modification trials rule out documenting dietary intervention as a viable prevention strategy. This leaves chemoprevention – prevention through the administration of chemically based drugs – as the most viable option for preventing prostate cancer. As my discussion of the BCPTs showed, this approach places most organisational control in the hands of a centralised group of cancer researchers; it will be

administered to the public by oncologists and will marginalise the professional skills of other health service providers.

A prostate cancer prevention trial (PCPT) began enrolment in the USA in October 1993. It is a double-blind placebo controlled clinical trial in which half of the participants are given an active agent (the enzyme-blocking drug finasteride) while the other half are given a placebo. The trial is being overseen by the Southwest Oncology Group. It involves around 220 sites across the USA, and is sponsored by the US National Cancer Institute which is providing approximately $60 million towards the trial expenses. Unlike the BCPT, the PCPT had no problems enrolling the 18 000 men it required. The trial is expected to take 10 years, with 3 years for enrolment and analysis, and 7 years for the treatment phase during which time men on the active arm of the trial will be asked to take 5 mg per day of finasteride (Allerton et al., 1998: 65; Coltman et al., 1999: 546; Reynolds, 1993: 1633).

Finasteride

Finasteride (trade name Proscar) is a drug which has been used to treat men with symptomatic non cancerous enlargement of the prostate, that is, benign prostatic hyperplasia (Brawley et al., 1994: 596). Following animal studies which suggested the drug has few negative side effects, a phase III Benign Prostatic Hypertrophy Trial was run in North America in which 895 men were treated with either placebo, 1 mg of finasteride per day, or 5 mg of finasteride per day. The results, which were published in 1992, were favourable, and the only side effects reported were a decrease in libido and a decrease of ejaculatory volume among those taking finasteride (Gormley et al., 1992). The FDA approved finasteride for the treatment of BPH in the same year (National Cancer Institute, 1999). Finasteride is a 'young' drug compared to tamoxifen, and it is possible that long term side effects are yet to

surface. It is a promising candidate for preventing prostate cancer because of its low toxicity and because it reputedly slows the growth of prostate cancer cells in a laboratory setting by blocking 5-α-reductase (Szarka et al., 1994: 41).

Finasteride was the first 5-α-reductase inhibitor to enter clinical trials (Brawley et al., 1994: 596), and is thought to control BPH by reducing local levels of dihydrotestosterone (DHT), the major androgenic compound found in the prostate gland (Szarka et al., 1994: 40). DHT is a compound produced from testosterone by the enzyme 5-α-reductase which binds with androgen receptor cells in the prostate resulting in cell growth. Although both testosterone and DHT can bind to the androgen receptor cells, DHT is thought to be a more powerful stimulant for cell growth: "When compared to [testosterone], DHT exhibits a higher binding affinity for and lower dissociation rate from the androgen receptor" (Brawley et al., 1994: 596). An absence or reduction of 5-α-reductase, as occurs in some types of male pseudohermaphroditism, is thought to result in an underdeveloped prostate gland and lower rates of both BPH and prostate cancer (Szarka et al., 1994: 40). The inhibition of 5-α-reductase hampers the conversion of testosterone into DHT.

The hypothesis behind the PCPT is that if finasteride can reduce the level of DHT in the prostate, it might also reduce the incidence of prostate cancer. Edward De Antoni and David Crawford write that:

> [s]cientific evidence for this hypothesis is circumstantial at best, with no proof that the pathogenesis of the disease can be affected by the manipulation of DHT. Nevertheless, this clinical trial is an important first step (De Antoni & Crawford, 1994).

The PCPT is far from being a 'first step' as it involves 18 000 men and costs over US $60 million. Interestingly, the link between diet and prostate cancer is also "circumstantial at best" (Brawer & Ellis, 1995: 1784) but the advocates of the PCPT still hold that in that instance the 'scientific evidence' does not warrant a clinical trial.

As discussed in Chapter 4, treatments used in prevention must be well tolerated and largely free of side effects. Two of the researchers directly involved in the PCPT trial write:

> In a number of clinical trials for the treatment of BPH, finasteride has been demonstrated to be a very safe drug with minimal side effects. Given its excellent safety profile and the possibility that it may also prevent BPH, finasteride would be very suitable for long-term administration as a cancer chemopreventive agent (Brawley et al., 1994: 596-7).

At 5 mg per day taken orally finasteride causes a 75 per cent decrease in serum DHT levels, an 80 per cent decrease in intra prostatic DHT, and a 10 per cent increase in serum testosterone. While high levels of testosterone can interact with androgen receptors in a manner similar to DHT (Placido et al., 1990: 1165-1171), Brawley and Thompson discount this elevation of testosterone as insignificant in causing prostate cancer growth (Brawley et al., 1994: 596). Given its ability to reduce serum DHT and its reported minimal side effects, in the eyes of the trialists finasteride fulfils the safety requirements for a preventative drug. Merck and Co., Inc. (Whitehouse Station, N.J.) will provide the drug and matching placebo free of charge for the duration of the trial (Reynolds, 1993: 1634).

Treatment and monitoring

In addition to testing whether finasteride can prevent prostate cancer, subsidiary objectives of the trial are to investigate the side effects associated with the drug, the frequency with which they occur, and to gauge whether its long term use by healthy men will be acceptable. Further, the effects of finasteride on the two major tests used to diagnose prostate cancer are unknown, so the trial will also evaluate the drug's impact on both the sensitivity and specificity of DRE and PSA screening (Feigl et al., 1995: 150-51).

A feature which stands out in medical discussions of the PCPT is the emphasis placed on the impact of the drug on sexual functioning. In the BPH study mentioned previously, proportionally more men taking finasteride than placebo experienced decreased libido, ejaculatory disorders, and impotence (Gormley et al., 1992: 1189-90). When discussing the design of the PCPT, Feigl et al., single out sexual function as the side effect requiring particular attention. It is reasonable to assume, they argue, that a negative impact on sexual function resulting from finasteride will be less tolerable in healthy men and perhaps younger men, than in men suffering the symptoms of BPH (Feigl et al., 1995: 158). That is, men may tolerate side effects if they have a medical condition but it is another matter for healthy men. This, in turn, may affect the compliance of participants.

Side effects will be specifically evaluated in the first 1800 men randomised into each arm of the trial, with both clinical and self-reported assessment being taken twice a year throughout the trial (Feigl et al., 1995: 158). Despite ongoing controversy over the accuracy of prostate needle-biopsy (Australian Health Technology Advisory Committee, 1996), at the end of seven years all trial participants will have a biopsy to establish whether they have prostate cancer, and

if so, what stage their cancers have reached. The cost of the analysis of blood samples for annual PSA tests and the analysis of the biopsy at the end of the trial will be covered by the NCI trial funding and a cholesterol screening test will also be provided, however participants are expected to cover the costs of annual DRE and PSA screening which are considered to be a normal part of health care (National Cancer Institute, 1999). In the 'Questions and Answers about the PCPT' sheet prepared for general readership and prospective participants, the trialists write that:

> The only charges to the participants will be for routine health care that all men in this age group should have. Physician, medical examination, and general clinical costs, including DREs and drawing blood for PSA testing, will be charged to the participant in the same way as if he were not part of the trial. However, the costs for these tests may be covered by a participant's health insurance. If cancer or other prostate problems are discovered during the regular exams, the participant will be referred to his personal physician for appropriate care. Costs for diagnosis and treatment of prostate problems, prostate cancer, or other medical conditions during the seven years of the study are also the responsibility of the participant (National Cancer Institute, 1999).

This quote indicates a number of assumptions that underpin the design of the trial. Initially, DREs and PSA sampling are requirements of the trial. Regardless of whether these measures are usually routine, they are factored in as mandatory monitoring points and men participating in the trial must bear their expense. Although in a biomedically ideal world all men over the age of 55 would routinely undergo annual examination, this is not the case in practice. In their report on

prostate cancer screening, the Australian Health Technology Advisory Committee did not establish a base line of the percentage or number of men being screened, suggesting that, in this country at least, these figures are not known or that screening is not currently standard practice (Australian Health Technology Advisory Committee, 1996). To include these procedures under the auspices of 'routine health care' obscures the controversies surrounding their use (see, for example, Small, 1993). As mentioned earlier these controversies include not only concern over the accuracy of screening techniques but also questions about the value of early detection of cancers given the limits of current treatments.

By utilising DRE, PSA screening and needle biopsy, the organisers of the PCPT are attempting to stabilise a specific instance of knowledge production through the application of standardised, broadly accepted measuring tools. The use of standardised tools aims at making the actions of scientists comparable "over time and space" (Timmermans & Berg, 1997: 273). The trialists are, then, attempting to link the 220 different trial sites by providing clinicians with highly mobile resources that, as Latour says, "make action at a distance possible" (Latour, 1987: 287). But in doing so the trialists are simultaneously working towards stabilising these uncertain technologies as unproblematic and transferable units of meaning, and, in order to achieve this, they are 'tinkering' with them to make them fit the local context (Casper & Clarke, 1998; Knorr-Cetina, 1981).

Consider the following problems surrounding the routine use of PSA screening in the prevention trial. The effects of finasteride will be measured using PSA to detect serum dihydrotestosterone levels. Although it is not universally accepted, the PSA blood test is becoming increasingly widespread as a screening tool. A PSA level above 4 ng/ml is typically used as an indication that further exploration,

such as a biopsy, is warranted. In the dose used in the PCPT, finasteride is reported to reduce serum PSA levels by approximately 50 per cent over the period of one year (Guess et al., 1993). As many as one third of men over the age of 50 are thought to have some histologic evidence of prostate cancer (Australian Health Technology Advisory Committee, 1996) so the use of PSA screening within the trial would need to be sensitive to a reduction in serum PSA resulting from finasteride, while not assuming this indicated an absence of any prostate abnormality. Failure to acknowledge the effect of the drug on PSA levels could result in a disproportionately small number of the men taking finasteride reaching the PSA level at which further exploration is recommended. If this occurred the cancer detection rate in the finasteride arm of the trial would be artificially low (regardless of whether finasteride actually prevents cancer) simply because men taking the drug would not be referred on for biopsies, and it is through biopsy that the presence of tumours is confirmed. If cancers were overlooked in men taking finasteride, the preventative effectiveness of the drug would be overestimated (Feigl et al., 1995: 152). By adjusting the use of PSA screening to account for these contingencies the standardised diagnostic technology is being made to fit the local context of knowledge production.

Similar ambiguities exist about the use of DRE among men taking finasteride. When given for six months finasteride is reported to reduce the size of the prostate by approximately 20 per cent. This reduction in prostate size has the potential to confuse clinicians administering DREs, as the size of a man's prostate is an indicator of its health. If the prostate shrinks at an even rate, resulting in a gland that is smooth to the touch, cancers may not be detected. If, however, the prostate contracts unevenly clinicians may detect lumps and bumps which they consider need follow-up. The result may be an increase in the number of tumours detected

with needle biopsy which would affect the outcome of the trial (Coltman et al., 1999: 545). Again, 'fine-tuning' the relationship between prostates, clinicians and needle biopsies, will be needed in order to sustain the DRE as a viable screening procedure.

The finasteride trialists have attempted to account for the ambiguities surrounding DREs and PSA testing by incorporating a numerical estimate of their effects (see for example Allerton et al., 1998; Coltman et al., 1999: 545). It should be noted, however, that these are estimates only, and in using these screening tools to monitor the impact of finasteride the trial sets up a relation between three technologies, all of whose effectiveness is currently uncertain. In so doing the trial helps institute the use of DRE and PSA as standard diagnostic tests for prostate cancer. In much the same way that the BCPTs relied on unstable technologies, such as the Gail risk model, the design of the PCPT is facilitating a 'locking in place' of these technologies so that each will benefit by its association with and reliance on the other and will appear 'more certain'.

Conclusion

This chapter has used the importance of gender for a notion of men's health to launch a discussion of the biomedical representation of prostate cancer. I argued that, once again, sex hormones are an important tool for the medical researchers trying to imagine a relationship between the body's interior environment and the occurrence of disease. But hormones are also a device which bridges this interior environment and the social and psychic constitution of masculinity. Because of this, technical discussions about specific risk profiles, the effectiveness of specific screening technologies, or the actions of drugs (which in the instances cited make reference to hormonal markers) are also discussions about the biomedical

construction and deployment of masculinity. As with the hormonally constituted subjectivity mobilised within the breast cancer prevention trials, this is a gendered identity which is specifically constrained by the mandate of science. The differences between the femininities and masculinities produced within the breast and prostate cancer literatures is the subject of the following chapter.

CHAPTER 7

Some reflections on gender difference in the medical construction of prostate cancer and breast cancer

The previous chapter has shown that there are many similarities between debates about the significance of gender for women's and men's health, the deployment of gender in the construction of male and female sex hormones, the role of sex hormones in the ongoing iteration of gender, and current representations of breast and prostate cancer. But significant differences also mark these debates. The grouping together of oppositional terms has a long history within Western intellectual traditions, and exposing the way these incorporate hierarchical representations of difference has been a major analytic strategy for feminists. While it may appear that these couplings are merely used to identify categories and the boundaries which separate them, in fact they mask a deeply ingrained privileging of one term over another (Shildrick, 1997: 105) and a polarisation which effectively excludes middle terms (Haraway, 1989: 12). Locating sex hormones within such a scheme provides a way of interrogating the specific construction of gender difference in the breast and prostate cancer trials.

The binary pair which form the foundation of Cartesian metaphysics, the mind / body split, provides the basis for dichotomies such as 'rationalism' and 'empiricism', 'subject' and 'object', and 'reason' and 'passion'. In these splits the primary term is always constructed as the referent to which the later, or 'marked' term, rather than simply being a conceptual partner, is somehow subordinate or inferior (Shildrick, 1997: 105). In such pairings terms are constructed as polar

opposites with no commonalities which could link them together or form a middle ground.

While a large number of terms can be coupled in ways that reflect this hierarchical organisation of difference, many of these will actually function as subsets of broader terms. In this way the privileging which occurs within some binary pairs is extended to other related terms. An obvious example of this is the binary pair 'male' and 'female', where 'female' is always the marked term and discursively constructed as inferior to the primary term 'male' (Shildrick, 1997: 106). 'Sex' and 'gender' and 'science' and 'nature' are other examples. Exploring the relationship between such hierarchically organised dichotomous couplings, and seeking to identify how and when positive or negative values became attached to the terms, has been a way for feminist scholars to unravel seemingly natural beliefs and demonstrate that they are in fact the product of specific historical moments and social constellations. According to Shildrick, it is the positioning of categories and concepts that have become attached to male identity against those attributed to female identity that need to be deconstructed (Shildrick, 1997: 107). How and why have qualities such as 'active', 'strong', 'objective' and 'independent' become marked as 'male' while their counterparts, 'passive', 'weak', 'subjective' and 'dependent', signify 'female'? In undertaking this task it is not simply a matter of gender stereotyping but of providing a detailed evaluation of how the female set has systematically been devalued, regardless of the characteristics it displays. This devaluing needs to be articulated for each specific example, but put in context so that individual qualities (such as female as 'nurturing') are located within a discourse of the systemic devaluing of female attributes. When the whole discourse is taken into account it becomes more likely that the 'male' term and its associated concepts, will be privileged (Shildrick, 1997: 107). The tension inherent

in the ordering of 'man' and 'woman', and 'sex' and 'gender' into an antagonistic hierarchy strongly indicates that feminist theory needs to analyse the construction of the natural sciences, and in particular the life sciences. According to Haraway, the discourses of biology and the natural sciences are pivotal technologies for mapping the borders between the material and social worlds (Haraway, 1989: 290).

For my purposes, the entities called 'sex hormones' are constitutive of the political and discursive tensions operating in these dichotomies. The coupling of 'androgens' and 'oestrogens' is a subset of the dualism male / female. It is the male hormone which is the dominant term, acting to constitute the female hormone as the displaced 'other'. Chapter 3 provided a number of examples of the attribution of positive and assertive characteristics to 'male' hormones and negative and passive characteristics to 'female' hormones, and tied these to historically and culturally constituted beliefs. The literature on the PCPT and the BCPTs provides another example of the way these beliefs are written into scientific accounts of the body.

Cancer is a disease which provokes profound cultural dread. Sontag had described how this dread is expressed through metaphors of chaos, corruption and insidious violence as the body betrays itself (Sontag, 1991). Because of the emphasis on the role of sex hormones in the cause, prevention and treatment of prostate cancer and breast cancer, both diseases can be read as metaphorical accounts of sexuality gone mad. These things called hormones, constituted as crucial elements of the essence of sex, become twisted, perverted, and turn back on the body in a malignant rampage. The portrayal of breast cancer incidence and risk can be interpreted through liberal feminist arguments that representations of female sexual pleasure

provide a map for interpreting gender politics. These accounts have, however, been criticised for falsely universalising female sexual pleasure and failing to consider cultural variance, in particular racialised symbolism around black women's sexuality which depicts them as more primitive and sexually intense than white women (Haraway, 1989: 355). Scientific representations of the relation between sex hormones and breast cancer contain a moral narrative about female sexuality: the sexually healthy white woman will be prudish and channel her desires through married heterosexual coupling aimed at reproduction while those whose desires extend beyond this are constituted as possessing an increasingly risky and dangerous sexuality. As discussed in Chapter 4, the representation of hormonal risk in the breast cancer literature mirrors a specific type of female sexuality; the woman at least hormonal risk is one who does not reach puberty too early, has several children while she is young and breastfeeds them, does not have any induced abortions and does not have a 'late' menopause. These specifications constitute and constrain 'healthy' female sexuality.

Racial factors also feature in the constitution of breast cancer risk categories. For a number of reasons which are not definitively understood, white women have a higher incidence than Japanese or African-American women. Because of biomedicine's racial gaze, Japanese or African-American women may possess the same hormonal markers as white women but not be constituted as 'at risk'. The white bourgeois west has historically inscribed the 'other' (whether they be racially or economically 'other') as naturally possessing an exotic, primitive, and insatiable sexuality (see, for example, Gilman, 1985; Stoler, 1997; Watney, 1990). For this reason, hormonal markers that indicate a dangerous excessive sexuality for white women, merely indicate the 'natural' (therefore unproblematic) uncontrollable animalistic sexuality of the dark woman.

But racial sexuality is also gendered, and while African-American women are not constituted as problematic within hormonal discourses of cancer risk the same is not true for African-American men. In the medical portrayal of prostate cancer white men are at less risk than Afro-American (see for example Coltman et al., 1999; Giovannucci, 1995). Interpreting this attribution of risk as a parable about sex and morality, the racialised constitution of the sexual proclivity of Afro-American men as threatening, aggressive, dangerous and cunning is reinforced (Haraway, 1989: 355; Watney, 1990). The link between prostate cancer and testosterone, and testosterone and aggression further inscribes black men as more influenced by the natural rather than the social order.

Testosterone is the primary hormonal signifier of the category 'male'. Bearing in mind the contingent nature of medical knowledge, it is a 'fact' that testosterone is doubly responsible for stimulating abnormal cell growth in the prostate both through binding with androgen receptor sites, and through providing the source material from which prostatic DHT is made. In the medical literature, however, testosterone is now distanced from prostate cancer and the majority of attention is focused on DHT. For example:

> The androgen dependence of early prostatic cancer is unequivocally established by its regression following castration... As such, castration is known to reduce circulating levels of testosterone by some 90%; it was assumed that testosterone was the key androgen in prostate and tumour growth. In the last decade it has become clear, however, that in so far as the prostate in concerned, 5α-dihydrotestosterone (DHT) and not testosterone is the main trophic hormone responsible for growth.... Thus, if testosterone represents the major endocrine support of the [cancer], then castration or its

> equivalent must, perforce, represent the treatment of choice. If, however, tumour growth depends upon DHT, then logically treatment must be directed towards elimination of DHT alone, leaving testosterone levels unchanged,… (Petrow et al., 1984: 352).

The justification for the increased focus on DHT is the belief that it is pharmacologically more potent than testosterone, but in shifting attention away from testosterone researchers have enacted a symbolic severing of the causal connection between male sexuality and the disease. If testosterone were seen as the main entity responsible for causing prostate cancer, then in a sense the 'essence of man' is implicated as somehow polluted and morbid. By shifting attention to DHT, testosterone remains untainted as a signifier of 'normal masculinity'. Further, the cumulative biological effects of a lifetime of sex (bearing in mind that sexual arousal and orgasm result in a short-term increase of testosterone) and the maintenance of sexuality as a man ages, are not constituted as pathological. This is in sharp contrast to the construction of the category 'female' and the way that oestrogen, including 'life-time exposure to oestrogen', is depicted as fundamentally unstable and problematic (see Chapter 3).

This disparity in the constitution of male and female sexuality is further amplified in the way 'normal sexuality' is portrayed in the prostate cancer and breast cancer literatures. Prostate cancer is a specifically sexed disease (even more so than breast cancer – from which men can and do suffer). Removal of the testes (which is standard treatment for advanced prostate cancer) will of course leave men impotent. Drug therapy which stops the production of testosterone (another standard treatment) also reduces libido and the ability to achieve an erection. And removal of the prostate or part of it (standard treatment for early or localised

prostate cancer) leads to impotence rates of between 30 and 80 per cent depending on how they are measured (Adami et al., 1994: 958). In addition, the hormonal effects of these treatments or treatment with synthetic hormones, can bring about an increase in oestrogen circulating in the blood and result in feminising changes in the pitch of a man's voice and enlarged breasts (Wasan & Waxman, 1992: 477). Questions about the effects of different treatments on men's sexuality are, therefore, undoubtedly of crucial importance. But in these accounts what is understood to be a 'healthy sexuality' assumes a certain physical type and a specific sex act. As discussed in Chapter 3, this physical type (the standard male norm) assumes a man has intact genitals and assumes the physical act of interest is penetrative intercourse ending in ejaculation, preferably of viable sperm. For example:

> If, as is highly probable, human prostatic cancer likewise depends upon DHT for endocrine support, then the way is open to new palliative therapy that avoids the trauma of castration. Such an approach is particularly attractive as lowered 5a-reductase levels do not affect fertility, or lead to the undesirable physiological/psychological side-effects that are characteristic of castration (Petrow et al., 1984: 352-3).

And:

> Pure antiandrogens such as the non-steroidal agent flutamide were developed as testosterone receptor antagonists but also suppress cortisol production and oestradiol conversion. The major advantage of these compounds is that potency is preserved (Wasan & Waxman, 1992: 477).

There are many parallels between the effects of treatments for breast cancer and prostate cancer. Despite this, representations of female sexuality within cancer medicine constitutes women's sexuality as dependent on servicing male pleasure, while men are constructed as rightful agents of their own sexuality. As the relevant literatures are so extensive it is difficult to demonstrate this persuasively without either digressing into a major systematic literature review or presenting highly selective (and possibly unrepresentative) examples. As a gross indicator I carried out a content analysis of Medline articles for breast cancer and prostate cancer, for the period 1990 (the time at which articles referencing the tamoxifen prevention trial began to appear) to April 2000. Such an analysis runs the risk of generating trite and overly simplistic outcomes and is beneficial to this thesis only because it adds texture to my reading of the gendered subjectivities produced within medical literature. I must also acknowledge that the key words used to compile this search are themselves gendered and work toward producing different outcomes for men and women. Rather than seeing this gendering as an obstruction, it is a point of interest: how can one inquire into the medical construction of sexuality without appealing to language which has a gendered history? The following table shows the key words used and the frequency with which they appeared in the literature:

Comparative representation of sexuality in the breast cancer and prostate cancer literature, 1990 to 2000:

Total medline hits	Breast Cancer 44890		Prostate Cancer 9303		ratio BC:PC
search term	no. of hits	%of total BC hits	no. of hits	% of total PC hits	
sexuality	49	.11	19	.21	1:1.9
libido	17	.03	1	.49	1:2.7
sexual pleasure	2	>.01	1	.01	1:2.4
orgasm	4	>.01	4	.04	1:4.8
infertility	74	.17	19 (impotence 146)	.21	1:1.2
sexual function	12	.02	81	.87	1:32.4
partner / husband	84	.19	partner / wife 9	.09	1:0.5

As can be seen from the table above, the key words of interest appear in only a very small proportion (usually comprising less than half a percent) of the total research on breast and prostate cancer. I have expressed them both as a percentage of the total number of Medline hits for the terms 'breast cancer' and 'prostate

cancer', and as a ratio of the frequency with which the terms occur. The key words used can be grouped into three loose themes which refer to different aspects of sexuality. These are personal sexuality and sexual pleasure (including the search terms 'sexuality', 'libido', 'sexual pleasure' and 'orgasm'), sexual performance and reproductive capacity (including the terms 'infertility', 'sexual function' and 'impotence'), and relation to an intimate partner (including the terms 'partner', 'wife' and 'husband'). Notions of sexual appetite and gratification (both attributes in which an active male sexuality are asserted) occur more often in the prostate cancer literature than in the breast cancer literature, ranging from 1.9 times more frequently for 'sexuality' to 4.8 times more frequently for 'orgasm'. In the second group, performance and reproductive capacity are constructed as more of an imperative for men than women, with the term 'sexual function' appearing 32.4 times more frequently in the prostate cancer literature. 'Infertility' also has a disproportionate representation (appearing 1.2 times in the prostate cancer literature for every mention in the breast cancer literature), although the inclusion of prostate cancer hits under 'impotence' (a specifically sexed term which combines notions of performance as well as reproductive failure, for which there is no female equivalent) once more exaggerates this difference. It is only when attention is turned to key words which are suggestive of a relationship with others that women once more come to the fore. The search 'partner / husband' retrieved twice as many hits in the breast cancer literature as the search 'partner / wife' retrieved in the prostate cancer literature, confirming that the sexual welfare of the sick woman's sexual partner is more salient in the literature than that of the man's sexual partner.

The above findngs tell us nothing particularly novel about breast cancer or prostate cancer, but they are representative of the assumptions made within, and reinforced

by, biomedical discourse about sexuality. Consider the issue of infertility. As discussed earlier, damage to fertility during cancer treatment is seen as a major problem for men, and while it is also a problem for women it is a different sort of problem. Breast cancer treatment options include mastectomy, removal of the ovaries and even removal of the uterus. Removal of the ovaries and uterus are, of course, female castration. They may be less outwardly visible than the removal of the testes, and less definitively tied to participation in sexual intercourse (as a woman can be penetrated regardless of whether she has ovaries, uterus or breasts), but their loss is castration nonetheless. Further, cessation of menstruation and induced menopause are common effects of radiation treatment and chemotherapy. While they are deemed an undesirable side effect of treatment, there is an assumption that women will not be fertile after a certain point in their lives, and indeed 'late pregnancy' is considered risky or even monstrous, so induced loss of fertility is seen as less of a problem and may even be marginally beneficial. While lost fertility following prostate cancer is constructed as a problem because it impedes men's ability to assert their sexuality through the heterosexual sex act and reproduction, the female body constructed in the breast cancer literature possesses a malignant, uncontrollable sexuality. Induced infertility among women with breast cancer will at least limit the ability of that sexuality to actively replicate its deviance.

The assertion that prostate cancer treatments are problematic because of their effect on sexual function again assumes a sexual function for men that is quite distinct from the sexual function of women. The active autonomy of male sexual pleasure is at the centre of prostate cancer literature through the premise that sexual function is dependent on men's ability to achieve an erection and ejaculate, and the effects of various treatments are gauged against this standard. While

mastectomy is the partial or full loss and stigmatisation of one of the primary socially coded sites of female sexual pleasure, the effects of mastectomy on female sexuality are frequently canvassed in the form of discussions about 'sexual rehabilitation' aimed at the resumption of heterosexual relations (Broom, in press). With this commentary I do not mean to undermine the maintenance of full sexual pleasure and function as a goal in development of prostate cancer treatments. Rather I simply point out that within cancer medicine, sexuality is defined and prioritised differently for women and men.

Medical researchers writing about prostate cancer attribute an agency to male sexuality and this agency is exerted most clearly in the performance of heterosexual intercourse. Within the discourses of medicine, testosterone and other androgens are constituted as being essential for male sexual performance and male performance is constituted as being crucial for 'normal' male sexual identity. This emphasis on the bodily enactment of sex complements writers such as Butler and Grosz, for whom the body is a transitional entity, in need of constant psychic and physical reinforcement (Butler, 1990; Butler, 1993; Grosz, 1994). In this iteration embodied identity is constituted by the corporeal exterior and the psychic interior, but is not reducible to a finite relation between them, nor is it ever complete. In particular the normalisation of gender is sustained through constant renewal and repetition in the form of actions and gestures which mark the body. The need for the continual reiteration of gender through bodily performance reveals the instability of gender (McNay, 1999). Within this constant remaking of embodied identity the psychological and physical effects of prostate cancer treatments both transgress normalised masculinity, and create a space for a novel masculinity to exist. At the start of the previous chapter I discussed the disavowal of vulnerability in dominant forms of contemporary masculinity; the symbolic importance of

believing that 'real men' don't get sick, and when they do, they don't complain (see chapter 6 of this thesis and Kimmel, 1995). The lived experience of prostate cancer, with its attendent leaky, medically subjugated body, requires a response as a man enacts the bodily preformance of his gender. The collective enactments men with prostate cancer can shift the boundaries of gender by the repeated assertion of masculinity within this exclusively male disease. In the preformance of their sickness, (leaks, possible inability to engage in heterosexual penetrative sex, and other transgressions of gender norms) men with prostate cancer can alter communal expectations and validate an unconventional preformance of gender by others.

In summary, the medical literature constructs testosterone as an essential element of male sexuality. Although testosterone is implicated in causing prostate cancer, men with prostate cancer and men at risk of prostate cancer are assumed to be rightful agents of their own sexuality. This sexuality is one in which the inability to get an erection or ejaculate is seen as a substantial problem to the individual, rather than being seen as an indication of the cultural importance placed on phallic performance in the heterosexual sex act. Cancer medicine openly advocates the priority that treatment should not impinge on this sexuality whereas women are assumed to do anything to control breast cancer. In contrast, the sexuality of women patients with breast cancer or at risk of breast cancer, is constructed as explicitly pathological and in need of containment. While normal male sexuality is constructed as 'healthy', normal female sexuality is constructed as inherently dangerous and prone to malignancy. The best way to control this corrupt sexuality is to remove its source which is oestrogen, breasts, and ovaries, or rehabilitate it to the norms of a passive heterosexuality.

These differences between male and female sexuality in the cancer literature are indicative of and help constitute the subjectivity of men and women in medicine generally and in experimental medicine in particular. A final example from the breast and prostate cancer prevention trials further illustrates this.

Masculinity, the military and the medical subject

The finasteride prevention trial had no difficulties in exceeding its recruitment target within the allotted two years. This is in sharp contrast with the BCPTs where problems attracting participants resulted in a reduction of the trial size and an extension of the enrolment period in both the North American and UK based trials. The reasons why this occurred highlight differences in the historical constitution of experimental medicine, gender and cancer. And these differences constrain the subject identities available to and taken up by those involved in the BCPTs and PCPT. Specifically, the historical allegiance between a (largely male) state sponsored military and experimental medicine, and the (possibly) more comfortable fit of men with the identity available to experimental subjects, contributed towards the successful enrolment of the PCPT.

In Chapter 2 I discussed the importance of the involvement of the military in the emergence of the RCT as an experimental form. In the finasteride prevention trial the historical legacy of the relationship between the military and scientific medicine can, again, be identified. The US Department of Defence is an active participant in the PCPT, with researchers at four Department medical centres contributing, and defence (and former defence) personnel comprising approximately 10 per cent of the total number of participants (Allerton et al., 1998: 65). As the main aim of military medicine is the preservation of a healthy fighting force and prostate cancer is largely a disease of older men, the participation of the

defence institutions may seem unusual; however the impact of the disease on recipients of US defence benefits is substantial and set to increase as existing and former servicemen age, making prostate cancer a major budgetary issue (Allerton et al., 1998: 66). Because of the financial advantages should the trial be successful, it is not only in the interest of the Department of Defence to ensure the trial reached its recruitment target, but also, that the right kind of participants were recruited. Allerton et al. comment that;

> [A major] reason for DOD [Department of Defence] participation in this prevention trial lies in the nature of the participants themselves. Active duty and retired military personnel and their beneficiaries are generally well-educated, highly motivated, committed individuals who are used to making intelligent, informed choices. This motivation and commitment helps assure compliance with study design (Allerton et al., 1998: 66).

As well as being 'well-educated' and 'highly motivated' this group possess two further characteristics which have a potential to contribute to the success of the trial. It is a requirement of service within the military that individuals take on the rhetoric of altruism and deference of personal gratification for the 'the greater good', whether this be the good of one's colleagues in the heat of battle or service of the national interest. The rhetoric of altruism is also fundamental to the way the medical profession talks about clinical trials, with subjects regularly being encouraged to view their participation as contributing toward the advancement of medical knowledge for the benefit of future generations. In addition, throughout their professional lives members of the military are conditioned to follow the instruction of those with authority. As it is defence personnel who are administering the PCPT to servicemen and ex-service men, in the setting of

military medical facilities, it is safe to assume that this professional conditioning will extend to participation in the trial. Both an appreciation for the rhetoric of altruism and a deference to authority are likely to enhance recruitment and compliance with trial protocols.

Further factors combine to provide men a more comfortable fit with the position of experimental subject. This thesis has discussed the traditional androcentrism of science and some of the ways it appears within scientific medicine. One example has been the marginalisation of women within clinical research; the historical exclusion of women from trial populations because of risks should they become pregnant, the belief that hormonal fluctuations may affect the workings of experimental drugs and make women less biologically stable, and the belief that women were less likely to comply fully with the requirements of a trial (see Chapter 2). At the same time the politicisation of the women's health movement has sensitised women, and made them educated health consumers who are no longer prepared to uncritically take on board the opinions of the medical profession. Although there are calls by women's health advocates for the rigorous evaluation of the effects of many standard and experimental treatments on women it is reasonable to assume that women remain cautious about participating in clinical trials. My chapters on experimental methodology in medicine and the BCPTs discuss specific ways that RCTs continue to disenfranchise women.

The men's health literature talks of the reluctance of many men to seek medical help when they are unwell. As a speculative enterprise I suggest that taking up a position in a medical experiment may be a way for men to engage with the medical profession in ways which reinforce, rather than challenge, their gendered subjectivity. Instead of transgressing masculine ideals by admitting physical and

psychological need when they seek medical treatment men can align themselves with the characteristics of a masculine science while they are participating in a trial. Rather than being personal vulnerabilities, their diseases, symptoms and side effects become necessary data for the progress of scientific medicine. The personal discomfort of disease is transformed into a gesture of altruistic suffering. Of course this suggestion makes unrealistic assumptions about men's abilities to detach themselves from their experience of disease. Nonetheless, it is a suggestion which fits with the Cartesian mind / body split wherein the mind (gendered masculine) is of prime significance while the body (often gendered feminine) is devalued or denied, a hegemonic masculinity that disavows psychic or physical embodiment and the vulnerability that entails, and feminist concerns about the gendered nature of the ideological and material practices of science and scientific medicine.

Finally, men as a group have been less subjugated within medicine than women apparently have. Calls for more attention to the health needs of men and boys differ politically from the claims made by the early women's health movement; men may have been badly served by a medical profession who ignored their specific health needs, but they were not explicitly oppressed by it. Because of this, initiatives in men's health, such as the PCPT, may be greeted more enthusiastically and less cautiously than similar initiatives in women's health - at one level the men's health simply needs to get runs on the board while feminist engagement with health suggests women are still concerned with changing the rules of the game.

CONCLUSIONS

In this thesis I have examined processes of legitimation in medicine, looking first at the story scientific medicine tells about itself, then moving on to examine how that story came about and how it maps onto the social world. I have done this by taking the characteristics generally awarded to scientific knowledge - characteristics such as 'truth', 'adequacy' and 'objectivity' - and examined how, and by whom, they were constituted. In other words, I have treated them as categories of inquiry (Shapin & Schaffer, 1985: 13-14).

Sociological critiques of clinical innovation move toward an understanding of how justification in medicine occurs by exploring the socially constituted nature of individual and professional identity and bringing a gendered critique of science to bear on the production of medical knowledge (Oakley, 1989). Work within the sociology of scientific knowledge can extend this by demonstrating the flexibility of the boundary between natural and social objects and natural and social knowledge. Clinicians need to keep 'doing scientific medicine', and this need must be respected by not reducing clinical practice into exclusively social explanations of justification and scientific rigour. In order to reduce the risk of allowing social determinism to replace scientific determinism, and to avert the potential collapse of the natural into the social it is useful to conceive of entities traditionally described as 'natural objects' as knowable to us only because of the historical and social constellations through which they gain expression. These reifications of social and historical meaning can in no sense simply be 'explained away', rather; they exist and exert their presence upon other natural objects in tangible ways.

Similarly, RCTs are a technological system which is historically and socially constituted through the alignment of physical artefacts, human activity, and knowledge (Law & Bijker, 1992). Inconsistencies abound in the ways this system is represented by medical scientists, particularly in the way researchers routinely smooth over the practical difficulties of carrying out clinical research, make them appear unproblematic, or obscure them altogether. The result is that RCTs portray the clinician as a cognitively and socially disembodied knower and the experimental subject as the psychically and historically disembodied object of knowledge. A critique of the RCT which acknowledges these inconsistencies and embraces them as a focus of analysis develops quite a different picture of the technological system, the players involved with it and the knowledges, practices, and objects it helps produce. Instead of products of a detached science they become historically, socially and politically situated. Further, the type of research design chosen by medical scientists also affects the production of knowledges, practices and objects. More than any other form of medical experimentation, RCTs are portrayed as incorporating the rhetorical benefits associated with science and the scientific method. But this perception, far from being self-evidently true, has been carefully crafted through a disavowal of the historical and social contingencies that surrounded its emergence and rise to power and continue to surround its use.

At the beginning of the twenty-first century RCTs are instrumental in the production of the human body. Recognising that accounts of medical science are grounded in historical and social practice also requires that the bodies they construct be viewed as culturally embedded projects. As the emergence of discourses about sex hormones and the insistence on sexually different male and female bodies demonstrates, factors that are not strictly rational and scientific always contribute to the explanatory success of biological theories. Acknowledging the social embeddedness of medical research

allows for an analysis of the political and ideological interests, as well as the historical contingencies, which influence and become incorporated into medical knowledge, practices and objects. The institutionalisation of a relationship between laboratory research on sex hormones and the clinical use of and feedback into that research is one example of this. The mobilisation of hormonal discourses to facilitate the production of specific types of embodied sexual difference is another.

In the tamoxifen breast cancer prevention trials and the finasteride prostate cancer trial, clinical researchers are attempting to gauge the interactions between technologies, beliefs and objects in what they consider to be the best possible way. They can only apply the methods of the RCT to hormonal drugs, human bodies and diseases which are coded male or female, because of the dense and rich histories which are reified into each of these entities and the relationships which connect them. For example, while the breast cancer prevention trials were justified on the grounds that tamoxifen was a promising treatment which required scientific evaluation, there was in fact a myriad of reasons for carrying out the trial. Acknowledging those reasons, such as the manoeuvring of different interest groups as they sought to maintain or extend the boundaries of their professional domain, provides a more accurate, though more complex, picture of medical innovation.

The controversy which surrounds the BCPTs bears many of the hallmarks which usually accompany controversy in science. These included a clash of professional interests (with their requisite attempts to claim cognitive authority over the subjects and methods of the trials), and a claiming and counter claiming over methodological issues including statistical criteria used to identify reference points for the trials. In addition, advocates and opponents of the trials attempted to separate social and political issues from technical ones and attributed problems (such as ethical questions

surrounding the treatment of well women and the IBIS trialists' criticisms of the early closure of the NASBP trial) as being politically motivated. In so doing they maintained an insistence that the 'science' involved with the trials was distanced from the social and political sphere. Although the finasteride prostate cancer prevention trial has not created a similar controversy, it nonetheless shows the importance of factors extraneous to science for the development of medical knowledge and practice. For example, the historical androcentrism of medical research and the involvement of the military in clinical trials aided recruitment for the PCPT, while women's disenfranchisement within the clinical research process hampered enrolment for the BCPT and continues to affect the perception that they are 'too hard' to study.

Recognising and utilising the dynamics at work in a scientific controversy broadens the strategic possibilities available to those wishing to intervene in research and policy debates. In the controversy surrounding the BCPTs the deploying of different notions of 'risk' was a way of demarcating professional territory. In medical discourse 'risk' is used to denote, as specifically as possible, the likelihood that individuals or groups will experience a nominated health condition. Incorporating the notion developed by Beck - that 'risk' is a direct product of the decay of modernity (Beck, 1992) - the 'risky' medical subject can be understood as the psychic and corporeal manifestation of the historical and cultural legacies of modernity. Minimising risk, rather than being a purely technical enterprise (such as medical management through the use of screening technologies and the consumption of synthetic hormones), also becomes a question of reflexive engagement with modernity and its cultural and social products.

Within the breast cancer and prostate cancer literature sex hormones are represented as posing a risk to the healthy individual in ways which reflect a specific type of

sexuality. There is, however, a disparity between the ways in which male and female sexuality are constructed. Specifically, oestrogen has been pathologised in relation to breast cancer, while there are moves to quarantine testosterone from being implicated as a cause of prostate cancer. One implication of this is the higher priority placed on maintaining 'normal sexuality' in the prostate cancer literature compared to the breast cancer literature, and the attribution of agency to male sexuality. Thus, scientific medicine actively participates in reinscribing male performance of heterosexual intercourse as an act of significant symbolic and physical importance. At the same time, however, the adoption of screening technologies such as PSA at once draws attention to the delicacy of the male body while also invoking normative standards of male embodiment which largely disavow the possibility of physiological or psychic frailty. The incontinent, impotent, medically subjugated man's relationship with his corporeal body disrupts expected notions of male embodiment, aligning him instead with an embodied subjectivity traditionally occupied by women.

Implications for future research

Because assumptions about gender, sexed bodies and the privilege of science are so deeply entrenched within western culture, multiple strategies are needed to engage with them. To begin with there is a continued need for theoretical critiques of all aspects of the production of medical knowledge from science and technology studies, sociology and gender studies, because an historical and sociological gaze sees things which may be invisible to a biomedical gaze. But to my mind, these critiques will be most useful if they are directed towards and engaged with the politics and organisational conditions governing clinical research and practice. There is an abundant literature about medicine within STS, women's studies, philosophy and cultural studies whose message is unattainable outside the academic disciplines and

whose relevance to the material practices of medicine is equally obscure. If social commentators wish to influence medicine in any way they must acknowledge the current dominance of quantitative methods and the practical benefits they offer clinicians, researchers and policy makers. Failure to do so will leave them speaking to themselves and not impacting on research or the field of practice. The history of medicine is replete with instances where people outside the profession led the way in transforming medicine. The stakes are too high for social theorists not to make their voice heard.

The rise of evidence based medicine can be read as an attempt to improve the standards of clinical research, but it can also be interpreted as a way of policing the boundaries of medical knowledge and practice by professionals who wish to maintain and enhance the prestige and social authority medicine enjoyed throughout the twentieth century. Steven Epstein points out that the ascendancy of the RCT occurred at a time when the consumer health movement and women's health movement were posing a serious challenge to medical authority and gaining access to the arenas in which medical decisions and policy are made (Epstein, 1996: 189-90). Willis and White show editorial policies which privilege certain types of evidence effectively stop entire genres of research from being published in prestigious medical journals (White & Willis, 1999: unpublished). The requirements of evidence based medicine work precisely to exclude all non-quantitative forms of medical knowledge, shrouding both the content and (provided clinicians act appropriately) the practice of medicine in the mantle of science. In so doing evidence based medicine attempts to cordon medicine off from social and political analysis, as if that could insulate it from social and political influence. It is necessary, therefore, to insist that leading medical researchers and theorists respect both the intellectual practices and insights of the humanities and social sciences and not (as too often happens) view them as an inferior

and irrelevant enterprise. The humanities and social sciences are robust intellectual traditions which contribute greatly to our cultural capital as a society and need in no way justify their existence through engagement with the medical profession. When immersed in the outcomes-driven world of public health it is important to remember this.

One means of intervening in the privileging of certain types of quantitative evidence would be to institute a pedagogical change in the training of medical students and policy makers. Medical students need to have their respect for the authority of natural science tempered so that they can engage properly with the uncertainty that is an unavoidable part of medical practice and research. One point at which such a change could occur would be to re-write text book narratives of the development of scientific medicine and the history of the RCT. An account of the RCT which discusses the historical and political contingencies surrounding its invention and use would diffuse the illusion of neutrality which all too often is assumed to accompany trial outcomes. Such a move would have profound ramifications for the perceived basis of clinical authority, as it would require clinicians to accept a personal moral responsibility for the forms in which they re-enact and reconstitute medicine rather than allowing them to rely on an abstract notion of truth as governing their practice. By this I do not imply that medical practitioners are or should be the arbiters of a disembodied universal morality. Instead I urge that medicine should develop a situated morality which acknowledges the historical and political nature of concepts such as equity, health and well-being. This might not change anything in terms of either patients or practitioners lived experience of illness or a clinical encounter, but it certainly would change the way arguments about medical knowledge and clinical authority happen.

Another consequence of situating moral judgements and notions of objectivity in these ways would be a change in the meaning of evidence based medicine' and a revaluation of a range of medical experimental methods. As medical researchers shift their quest from being a search for truth and generalisability, into a recognition of diversity and a search for themes and meanings, so too will experimental methods need to evolve so as to cease doing symbolic violence to the diversity of research subjects' experiences as they are reduced to a common denominator. Medical researchers would be liberated to use a much richer 'tool kit' if the tyranny of the RCT were reigned in.

Bibliography

Abraham, J., (1995), *Science, politics and the pharmaceutical industry: Controversy and bias in drug regulation*, London, UCL Press.

Adami, H.-O., Baron, J.A. and Rothman, K.J. (1994), 'Ethics of a prostate cancer screening trial', *Lancet*, 343, 958-60,

Allerton, J., Seay, T., Optenberg, S., Coltman, C.A., Higgins, B., Thompson, I. and Lovato, L. (1998), 'Army and Air Force leadership in the prostate cancer prevention trial', *Urology*, 51 (Supplement 4A), April, 64-66,

Angell, M. (1993), 'Caring for women's health – what is the problem?', *New England Journal of Medicine*, 329, 4, 329-30,

Armstrong, D. (1977), 'Clinical sense and clinical science', *Social Science and Medicine*, 11, 599-601,

Assaf, A.R. and Carleton, R.A. (1998), 'The women's health initiative clinical trial and observational study: History and overview'.http://biomed.brown.edu/Other_ Information/RIMedicine/DecArt2.html, last updated 3 August, 1998, accessed September 1998.

Ault, A. and Bradbury, J. (1998), 'Experts argue about tamoxifen prevention trial', *Lancet*, 351, April 11, 1107,

Australian Health Technology Advisory Committee (1996), 'Prostate Cancer Screening', Commonwealth Department of Health and Family Services.

Bailar, J.C. (1983), 'Introduction', in Shapiro, S. and Louis, T. (eds.), *Clinical Trials: Issues and approaches*, New York, Marcel Dekker.

Barash, D. (1979), *The Whisperings Within*, New York, Harper and Row.

Barnes, B. (1977), *Interests and the Growth of Knowledge*, London, Routledge & Kegan Paul.

Barnes, B. (1985), *About Science*, Oxford, Basil Blackwell.

Barnes, B. (1990), 'Sociological theories of scientific knowledge', in Olby, R.C., Cantor, G.N., Christie, J.R.R. and Hodge, M.J.S. (eds.), *Companion to the History of Modern Science*, London, Routledge.

Barnes, B. and McKenzie, D. (1979), *On the Role of Interests in Scientific Change*, Keele, University of Keele Press.

Bates, E. and Lapsley, H. (1985), *The Health Machine: The impact of medical technology*, Victoria, Penguin Books.

Batt, S. (1994), *Patient no More: The politics of breast cancer*, London, Scarlet Press.

Batt, S. (1998), 'Tamoxifen and healthy women: That ol' black medicalization that we know so well', *DES Action Canada Newsletter*, 56, 2-6,

Baum, M. (1998), 'Cultural bias in the tamoxifen trials and tribulations', *Medicine and Culture Update: International differences, outcomes and values*, 2, 2, 7-8,

Bayer, R. (1981), *Homosexuality and American Psychiatry: The politics of diagnosis*, New York, Basic.

Beaglehole, R. and Bonita, R. (1997), *Public Health at the Crossroads: Achievements and prospects*, Cambridge, Cambridge University Press.

Beatson, G.T. (1896), 'On the treatment of inoperable cases of carcinoma of the mamma: Suggestions for a new method of treatment with illustrative cases', *Lancet*, 2, July 11,

Beck, U. (1992), *Risk Society: Towards a new modernity*, London, SAGE Publications.

Bell, S. (1987), 'Changing Ideas: The medicalisation of menopause', *Social Science and Medicine*, 24, 6,

Bloor, D. (1976), *Knowledge and Social Imagery*, London, Routledge and Kegan Paul.

Bordo, S. (1990), 'Reading the slender body', in Jacobus, M., Keller, E.F. and Shuttleworth, S. (eds.), *Body/Politics: Women and the discourses of science*, New York, London, Routledge.

Borell, M. (1976), 'Organotherapy, British physiology, and discovery of the internal secretions', *Journal of the History of Biology*, 9, 2, 235-268,

Borell, M. (1985), 'Organotherapy and the emergence of reproductive endocrinology', *Journal of the History of Biology*, 18, 1, 1-30,

Brawer, M.K. and Ellis, W.J. (1995), 'Chemoprevention for Prostate Cancer', *Cancer (Supplement),* 75, 7,

Brawley, O.W., Ford, L.G., Thompson, I., Perlman, J.A. and Kramer, B.S. (1994), '5-a-Reductase Inhibition and Prostate Cancer Prevention', *Cancer Epidemiology, Biomarkers & Prevention*, 3, 177-182,

Brind, J. (1999), 'Can abortion trigger cancer?', *Australian Doctor*, June 18, 73,

Broom, D. (1994), 'Taken down and used against us: Women's health centres', in Waddell, C. and Petersen, A.R. (eds.), *Just health: Inequality in illness, care and prevention*, Melbourne, Churchill Livingstone.

Broom, D. (1998), 'Facing facts, facing futures: Challenges to women's health', *Australian Journal of Primary Health - Interchange*, 4, 3, 40-49,

Broom, D. (in press), 'Reading breast cancer: Reflections on a dangerous intersection', *Health*, in press,

Broom, D. and Woodward, R. (1996), 'Medicalisation Reconsidered: Toward a collaborative approach to care', *Sociology of Health and Illness*, 18, 3, 357-378,

Brumberg, J.J. (1988), *Fasting Girls: The emergence of anorexia nervosa as a modern disease*, Cambridge, Harvard University Press.

Buchbinder, D. (1996), 'Men's troubles: The social construction of masculinity and men's health', *National men's health conference*, 10-11 August 1995, Canberra, Australian Government Publishing Service.

Bull, J.P. (1959), 'The historical development of clinical therapeutic trials', *Journal of Chronic Disease*, 10, 218-248,

Bulpitt, C.J. (1983), *Randomised Controlled Clinical Trials*, The Hague, Boston, London, Martinus Nijhoff Publishers.

Bush, T.L. and Helzlsouer, K.J. (1993), 'Tamoxifen for the primary prevention of breast cancer: A review and critique of the concept and trial', *Epidemiologic Reviews*, 15, 1, 233-43,

Butler, J. (1990), *Gender Trouble: Feminism and the subversion of identity*, London, Routledge.

Butler, J. (1993), *Bodies that Matter: On the discursive limits of sex*, London, Routledge.

Butler, J.R.G. (1997), 'The economic potential of tamoxifen prophylaxis in breast cancer', *Pharmacoeconomics*, 12, 3, 303-306,

Cadbury, D. (1997), *The feminization of nature: Our future at risk*, London, Penguin Books.

Callon, M. (1987), 'Society in the Making: The study of technology as a tool for sociological analysis', in Bijker, W.E., Hughes, T.P. and Pinch, T.J. (eds.), *The Social Construction of Technological Systems: New directions in the sociology and history of technology*, Massachusetts, MIT Press.

Cameron, D. and Fraser, E. (1994), *Masculinity, sexual violence and murder*, Cambridge, Polity Press.

CancerNet News, 1996, 'Breast cancer prevention trial will need fewer women for completion', last updated September 10, 1996, accessed July 1997.

Casper, M.J. and Clarke, A.E. (1998), 'Making the Pap Smear into the 'Right Tool' for the Job: Cervical cancer screening in the USA, circa 1940-95', *Social Studies of Science*, 28, 2, 255-289,

Castel, R. (1991), 'From dangerousness to risk', in Burchell, G., Gordon, C. and Miller, P. (eds.), *The Foucault Effect: Studies in governmentality*, Hemel Hempstead, Harvester Wheatsheaf.

Chesler, P. (1972), *Women and Madness*, Garden City, Doubleday.

Chetwynd, J. and Hartnett, O. (eds.) (1977), *The Sex Role System: Psychological and sociological perspectives*, Routledge & Kegan Paul, London.

Ching, C.K., Smith, P.G. and Long, R.G. (1992), 'Tamoxifen associated hepatocellular damage and agranulocytosis', *Lancet*, 2, 940,

Clark, S. (1993), 'Prophylactic tamoxifen', *Lancet*, 342, 168,

Clinical Oncology Society of Australia, Group, et al., (1994), 'Consensus report from Australia's first national breast cancer consensus conference', Clinical Oncology Society of Australia, Australian-New Zealand Breast Cancer Trials Group, Medical Oncology Group of Australia, Breast Section Royal Australasian College of Surgeons,.

Cohen, I., Rosen, D., Shapira, J., Cordoba, M., Gilboa, S., Altaras, M., Yigael, D. and Beyth, Y. (1994), 'Endometrial changes with tamoxifen: Comparison between tamoxifen treated and nontreated asymptomatic, postmenopausal breast cancer patients', *Gynecologic Oncology*, 52, 185-190,

Colborn, T., Domanoski, D. and Myers, J.P. (1996), *Our stolen future: Are we threatening our fertility, intelligence, and survival? A scientific detective story*, New York, Dutton.

Collins, H. (1985), *Changing Order: Replication and induction in scientific practice*, London, Sage.

Collins, H.M. (1982), 'The replication of experiments in physics', in Barnes, B. and Edge, D. (eds.), *Science in Context: Readings in the sociology of science*, Milton Keynes, The Open University Press.

Coltman, C.A., Thompson, I.M. and Feigl, P. (1999), 'Prostate Cancer Prevention Trial (PCPT) update', *European Urology*, 35, 544-547,

Connell, R.W. (1987), *Gender and Power*, North Sydney, Allen & Unwin Australia.

Connell, R.W. (1992), 'A Very Straight Gay: Masculinity, homosexual experience, and the dynamics of gender', *American Sociological Review*, 57, 735-751,

Connell, R.W. (1997), 'Australian masculinities, health and social change', in Huggins, A. (ed.), *Conference proceedings: Second national men's health conference*, Perth, Curtin University of Technology.

Conrad, P. (1975), 'The discovery of hyperkinesis: Notes on the medicalization of deviant behavior', *Social Problems*, 23, 12-21,

Conrad, P. (1992), 'Medicalization and Social Control', *Annual Review of Sociology*, 18, 209-32,

Conrad, P. and Schneider, J.W. (1980), 'Looking at levels of medicalization: a comment on Strong's critique of the thesis of medical imperalism', *Social Science and Medicine*, 14A, 75-79,

Cozzens, S.E. and Woodhouse, E.J. (1995), 'Science, government, and the politics of knowledge', in Jasanoff, S., Markle, G.E., Petersen, J.C. and Pinch, T. (eds.), *Handbook of Science and Technology Studies*, London, Sage.

Dabbs, J.M., Jurkovic, G.J. and Frady, R.L. (1991), 'Salivary testosterone and cortisol among late adolescent male offenders', *Journal of Abnormal Child Psychology*, Aug 19, 4, 469-78,

De Antoni, E. and Crawford, E.D. (1994), 'Strategies: Prevention, early detection, treatment of prostate cancer', *New perspectives in cancer diagnosis and management,* 2, 1,

De Gregorio, M.W. and Weibe, V.J. (1994), *Tamoxifen and Breast Cancer: What everyone should know about the treatment of breast cancer*, New Haven & London, Yale University Press.

Donegan, W.L. and Spratt, J.S. (eds.) (1988), *Cancer of the Breast*, W.B. Saunders Company, Philadelphia.

Douglas, M. (1984), *Purity and Danger: An analysis of the concepts of pollution and taboo* (first published 1966 Edition), London, Ark Paperbacks.

Dreger, A.D. (1998), 'A History of Intersexuality: From the age of gonads to the age of consent', *The Journal of Clinical Ethics*, 9, 4, 345-355,

Dresser, R. (1992), 'Wanted single, white male for medical research', *Hastings Center Report*, January-February, 24-29,

Early Breast Cancer Trialists Collaborative Group (1992), 'Systemic treatment of early breast cancer by hormonal, cytotoxic, or immune therapy: 133 randomised

trials involving 31,000 recurrences and 24,000 deaths among 75,000 women.', *Lancet*, 339, 8784, 1-15,

Economist, (1996), 2nd March, 83-84, 'Abortion, breast cancer, and the misuse of epidemiology', The Economist, 2nd March, 83-84,

Ehrenreich, B. and English, D. (1976), *Witches, Midwives and Nurses: A history of women healers*, London, Writers & Readers.

Ehrenreich, B. and English, D. (1978), *For Her Own Good*, New York, Anchor Press.

Ehrhardt, A. and Myer-Bahlburg, H. (1981), 'Effects of prenatal sex hormones on gender-related behavior', *Science*, 211, 20 March,

Epstein, S. (1996), *Impure Science: AIDS, activism and the politics of knowledge*, Berkeley, University of California Press.

Faulder, C. (1992), 'Better safe than sorry', *Bulletin of Medical Ethics*, February 1992, 29-33,

Fausto-Sterling, A. (1985), *Myths of Gender: Biological theories about women and men* (2nd edition 1992, Edition), New York, Basic Books, Inc.

Fausto-Sterling, A. (1993), 'The Five Sexes: Why male and female are not enough', *The Sciences*, March/April,

Fee, E. (1986), 'Critiques of modern science: The relationship of feminism to other radical epistemologies', in Bleier, R. (ed.), *Feminist Approaches to Science*, Oxford, Permagon Press.

Feigl, P., Blumenstein, B., Thompson, I., Crowley, J., Wolf, M., Kramer, B.S., Coltman, C.A., Brawley, O.W. and Ford, L.G. (1995), 'Design of the prostate cancer prevention trial (PCPT)', *Controlled Clinical Trials*, 16, 150-163,

Feinstein, A. (1989), 'Epidemiologic analyses of causation: The unlearned scientific lessons of randomized trials', *Journal of Clinical Epidemiology*, 42, 6, 481-489,

Feinstein, A.R. (1985), *Clinical Epidemiology: The architecture of clinical research*, Philadelphia, London, Toronto, Mexico City, Rio de Janeiro, Sydney, Tokyo, W.B. Saunders Company.

Fentiman, I.S. (1989), 'The endocrine prevention of breast cancer', *British Journal of Cancer*, 60, 1, 12-4,

Fingarette, H. (1988), *Heavy Drinking: The myth of alcoholism as a disease*, Berkeley, University of California Press.

Fleck, L. (1979), *Genesis and Development of a Scientific Fact*, Chicago, University of Chicago Press.

Fletcher, R. (1996), 'Testosterone poisoning or terminal neglect? The men's health issue', Canberra, Department of the Parliamentary Library.

Ford, L.G., Brawley, O.W., Perlman, J.A., Nayfield, S.G., Johnson, K.A. and Kramer, B.S. (1994), 'The potential for hormonal prevention trials', *Cancer*, 74 (supp), 9, 2726-2733,

Fornander, T., Rutqvist, L.E., Sjobert, H.E., Blomquist, L., Mattsson, A. and Glas, U. (1990), 'Long-term adjuvant tamoxifen in early breast cancer: Effects on bone

mineral density in postmenopausal women', Journal of Clinical Oncology, 8, 1019-24.

Foucault, M. (1977), *Discipline and Punish: the birth of the prison*, London, Allen Lane.

Foucault, M. (1980), *The History of Sexuality, Volume 1: An Introduction*, New York, Vintage Books.

Foucault, M. (1980), *Herculine Bardin: Being the recently discovered memoirs of a nineteenth century French hermaphrodite*, Brighton, Harvester Press.

Fugh-Berman, A. and Epstein, S. (1992), 'Tamoxifen: Disease prevention or disease substitution', *Lancet*, 340,

Gail, H.M., Brinton, L.A., Byar, D.P., Corle, D.K., Green, S.B., Schairer, C. and Mulvihill, J.J. (1989), 'Projecting individualized probabilities of developing breast cancer for white females who are being examined annually', *Journal of the National Cancer Institute*, 81, 1,

Gallagher, C. and Laqueur, T. (1987), *The Making of the Modern Body: Sexuality and society in the nineteenth century*, Berkeley, University of California Press.

Gibbs, W.W. (1998), 'The Prevention Pill', *Scientific American*, 278, June, 14-15,

Gilman, S.L. (1985), 'Black Bodies, White Bodies: Toward an iconography of female sexuality in late nineteenth-century art, medicine, and literature', in Gates, H.L. (ed.), *'Race', Writing and Difference*, Chicago, London, University of Chicago Press.

Giovannucci, E. (1995), 'Epidemiologic Characteristics of Prostate Cancer', *Cancer (Supplement),* 75, 7, 1766-1777,

Goffman, E. (1961), *Asylums: Essays on the social situation of mental patients and other inmates* (1968 Edition), Middlesex, Penguin Books.

Goldberg, S. (1993), *Why men rule: A theory of male dominance* (Revised edition of: The inevitability of patriarchy. 1977 Edition), Chicago, Open Court.

Goodare, H. (1993), 'Tamoxifen trial in healthy women at risk of breast cancer', *Lancet*, 342, 8868,

Gordon, J. and Ruddle, F. (1981), 'Mammalian gonadal determination and gametogenesis', *Science*, 211, 20 March,

Gormley, G.J., Stoner, E., Bruskewitz, R.C., Imperato-McGinley, J., Walsh, P.C., McConnell, J.D., Andriole, G.L., Geller, J., Bracken, B.R., Tenover, J.S., Vaughn, E.D., Pappas, F., Taylor, A., Binkowitz, B. and Ng, J. (1992), 'The effect of finasteride in men with benign prostatic hyperplasia', *New England Journal of Medicine*, 327, 17, 1185-91,

Gotfredson, A., Christiansen, C. and Palshof, T. (1984), 'The effect of tamoxifen on bone mineral content in premenopausal women with breast cancer', *Cancer*, 53, 853-57,

Grace, V.M. (1994), 'What is a health consumer?', in Waddell, C. and Petersen, A.R. (eds.), *Just Health: Inequality in illness, care and prevention*, Melbourne, Churchill Livingston.

Green, F.H.K. (1954), 'The Clinical Evaluation of Remedies', *Lancet*, 267, 1085-91,

Grosz, E. (1994), *Volatile Bodies: Toward a corporeal feminism*, Sydney, Allen & Unwin.

Grove, A. (1996), 'Taking on Prostate Cancer', *Fortune*, May 13, 35-42,

Groveman, A.A. (1998), 'The Hanukka Bush: Ethical implications in the clinical management of intersex', *Journal of Clinical Ethics*, 9, 4, 356-359,

Guess, H.A., Heyse, J.A. and Gormley, G.G. (1993), 'The effect of finasteride on prostate specific antigen in men with benign prostatic hyperplasia', *Prostate*, 22, 31-37.

Haraway, D. (1988), 'Situated Knowledges: The science question in feminism and the privilege of partial perspective', *Feminist Studies,* 14,3.

Haraway, D. (1989), *Primate visions: Gender, race and nature in the world of modern science*, London, New York, Routledge.

Haraway, D. (1997), Modest_Witness@Second_Mellennium.FemaleMan_meets_ Oncomouse: feminism and technoscience, New York, Routledge.

Harding, S. (1986), *The Science Question in Feminism*, Milton Keynes, Open University Press.

Harding, S. (1990), 'Feminism, Science, and the Anti-Enlightenment Critiques', in Nicholson, L.J. (ed.), *Feminism/Postmodernism*, New York, London, Routledge.

Harlap, S. (1992), 'The benefits and risks of hormone replacement therapy: An epidemiological overview', *American Journal of Obstetrics and Gynaecology*, 166, 6,

Harrison, J., Chin, J. and Ficarotto, T. (1992), 'Warning: Masculinity may be dangerous to your health', in Kimmel, M. and Messner, M. (eds.), *Men's Lives*, New York, Toronto, Macmillan.

Hartsock, N. (1990), 'Foucault on power: A theory for women?', in Nicholson, L.J. (ed.), *Feminism/ Postmodernism*, New York, London, Routledge.

Haseltine, F. and Ohno, S. (1981), 'Mechanisms of Gonadal Differentiation', *Science*, 211, 20 March,

Hearst, N. and Hulley, S.B. (1988), 'Using Secondary Data', in Hulley, S.B. and Cummings, S.R. (eds.), *Designing Clinical Research*, Baltimore, Hong Kong, London, Sydney, Williams & Wilkins.

Hennekens, C.H. and Buring, J.E. (1987), *Epidemiology in Medicine*, Boston, Toronto, Little Brown & Company.

Hennessy, R. (1993), *Materialist Feminism and the Politics of Discourse*, New York, London, Routledge.

Hill, A.B. (1951), 'The Clinical Trial', *British Medical Bulletin*, 7, 4, 278-282,

Hill, P., Wynder, E.L., Garbaczewski, L., Garnes, H. and Walker, A.R. (1979), 'Diet and urinary steroids in black and white North American men and black South African men', *Cancer Research*, 39, 5101-5105,

Holmes, H.B., Hoskins, B.B. and Gross, M. (1980), *Birth Control and Controling Birth*, New Jersey, Humana Press.

Howe, E.G. (1998), 'Intersexuality: What should careproviders do now', *Journal of Clinical Ethics*, 9, 4, 337-344,

Hunt, K. (1994), 'A 'cure for all ills'? Constructions of menopause and the chequered fortunes of hormone replacement therapy', in Wilkinson, S. and Kitzinger, C. (eds.), *Women and health: feminist perspectives*, London, Taylor and Francis.

Hunter, K.M. (1991), *Doctors' Stories: The narrative structure of medical knowledge*, Princeton, New Jersey, Princeton University PRess.

Illich, I. (1977), *Limits to Medicine, Medical Nemesis: the expropriation of health*, New York, Penguin Books.

Jasanoff, S., Markle, G.E., Petersen, J.C. and Pinch, T. (1995), *Handbook of Sciece and Technology Studies*, Thousand Oaks, California, SAGE Publications.

Jordan, V.C. (1992), 'Overview from the international conference on long-term tamoxifen therapy for breast cancer', *Journal of the National Cancer Institute*, 84, 4, 231-4,

Jordanova, L. (ed.) (1986), *Languages of Nature: Critical essays on science and literature*, Free Association Books, Worchester.

Kaufert, P. and McKinlay, S. (1985), 'Myth and the menopause', *Sociology of Health and Illness*, 4, 2,

Kavanagh, A.M. and Broom, D.H. (1998), 'Embodied risk: My body, myself?', *Social Science and Medicine*, 46, 3, 437-444,

Keller, E. (1982), 'Feminism and Science', *Signs: Journal of Women in Culture and Society*, 7, 3, 589-602,

Keller, E. (1983), *A Feeling for the Organism: The life and work of Barbra McClintock*, New York, Freeman.

Kelsey, J.L. (1993), 'Breast cancer epidemiology: Summary and future directions', *Epidemiologic Reviews*, 15, 1, 256-263,

Kemper, T.D. (1990), *Social structure and testosterone: Explorations of the socio-bio-social chain*, New Brunswick and London, Rutgers University Press.

Kesley, J.L., Gammon, M.D. and John, E.M. (1993), 'Reproductive factors and breast cancer', *Epidemiologic Reviews*, 15, 1, 36-47,

Kessler, S.J. (1990), 'The Medical Construction of Gender: Case management of intersexed infants', *Signs: Journal of Women in Culture and Society*, 16, 11, 3-26,

Keville, T.D. (1994), 'The invisible woman: Gender bias in medical research', *Women's Rights Law Reporter*, 15, 2 & 3, 123-142,

Kimmel, M. (1995), 'Series editor's introduction', in Sabo, S. and Gordon, D.F. (eds.), *Men's health and illness: Gender, power and the body*, Thousand Oaks, London, New Delhi, Sage Publications.

Knorr-Cetina, K. and Mulkay, M. (1983), *Science Observed: Perspectives on the social study of science*, London, Sage.

Knorr-Cetina, K.D. (1981), *The Manufacture of Knowledge*, Oxford, Permagon Press.

Kriegsfeld, L.J., Dawson, T.M., Dawson, V.L., Nelson, R.J. and Snyder, S.H. (1997), 'Aggressive behavior in male mice lacking the gene for neuronal nitric oxide synthase requires testosterone', *Brain Research*, 769, 1, 66-70,

Kuhn, T.S. (1970), *The Structure of Scientific Revolutions* (2nd Edition), Chicago and London, University of Chicago Press.

Kunkel, S.R. and Atchley, R.C. (1996), 'Why gender matters: Being female is not the same as not being male', *American Journal of Preventive Medicine*, 12, 5, 294-96,

Laing, R.D. (1976), *Sanity, Madness, and the Family*, Harmondsworth, Penguin.

Lancet, (1992), 339, 735, 'Tamoxifen trial controversy', editorial,

Laqueur, T. (1987), 'Orgasm, generation, and the politics of reproductive biology', in Gallagher, C. and Laqueur, T. (eds.), *Making of the Modern Body: Sexuality and society in the nineteenth century*, Berkeley, University of California Press.

Laqueur, T. (1990), *Making Sex: Body and gender from the Greeks to Freud*, Cambridge, Massachusetts, Harvard University Press.

Last, J.M. (1988), *A dictionary of epidemiology* (Second Edition), New York, Oxford University Press.

Latour, B. (1987), *Science in Action: How to follow scientists and engineers through society*, Milton Keynes, Open University Press.

Latour, B. and Woolgar, S. (1979), *Laboratory Life: The social construction of scientific facts*, California, Sage.

Laurence, L. and Weinhouse, B. (1994), *Outrageous Practices: The alarming truth about how medicine mistreats women*, New York, Fawcette Columbine.

Law, J. (1994), *Organizing Modernity*, Oxford, Blackwell Publishers.

Law, J. (1996), 'Organizing accountabilities: Ontology and the mode of accounting', in Munro, R. and Mouritsen, J. (eds.), *Accountability: Power, ethos and the technologies of managing*, London, International Thomson Business Press.

Law, J. and Bijker, W.E. (1992), 'Technology, stability and social theory', in Law, J. and Bijker, W.E. (eds.), *Shaping technology - Building society: Studies in sociotechnical change*, Cambridge, MIT Press.

Lawrence, C. (1995), 'National Men's Health Conference official opening', *National Men's Health Conference*, Australian Government Publishing Service, Canberra.

Leeson, J. and Gray, J. (1978), *Women and Medicine*, London, Travistock.

Legha, S.S. (1988), 'Tamoxifen in the treatment of breast cancer', *Annals of Internal Medicine*, 109, August, 219-228,

Levy, B. (1991), 'Bridging the gap in gender research', *Clinical Pharmacological Therapies*, 50, 641-6,

Long-Hall, D. and Glick, T. (1976), 'Endocrinology: A brief introduction', *Journal of the History of Biology*, 9, 2, 229-233,

Longino, H.E. (1990), *Science as Social Knowledge: Values and objectivity in scientific inquiry*, Princeton, New Jersey, Princeton University Press.

Love, R., Mazees, R.B., Tormey, D.C., Barden, H.S., Newcomb, P.A. and Jordan, V.C. (1988), 'Bone mineral density in women with breast cancer treated with adjuvant tamoxifen for at least two years', *Breast Cancer Research and Treatment*, 12, 279-302,

Love, R., Mazess, R.B., Barden, H.S., Epstein, S., Newcomb, P.A., Jordan, V.C., Carbone, P.P. and DeMets, D.L. (1992), 'Effects of tamoxifen on bone mineral density in postmenopausal women with breast cancer', *New England Journal of Medicine*, 326, 852-56,

Lupton, D. (1993), 'Risk as moral danger: The social and political functions of risk discourse in public health', *International Journal of Health Services*, 23, 3, 425-435,

Magriples, U., Naftolin, F., P E Schwartz, P., E and Carcangui, L. (1993), 'High-grade endometrial carcinoma in tamoxifen-treated Breast cancer patients', *Journal of Clinical Oncology*, 11, 3 (March),, 485-490,

Marks, H.M. (1988), 'Notes from the Underground: The social organization of therapeutic research', in Maulitz, R.C. and Long, D.E. (eds.), *Ground Rounds: One hundred years of internal medicine*, Philadelphia, University of Pennsylvania Press.

Marks, H.M. (1997), *The Progress of Experiment: Science and therapeutic reform in the United States, 1900-1990*, Cambridge, Cambridge University Press.

Martin, E. (1987), *The Woman in the Body: A cultural analysis of reproduction,* Boston Mass, Beacon.

Martin, E. (1996), 'The egg and the sperm: How science has constructed a romance based on sterotypical male-female roles', in Sargent, C.F. and Brettell, C.B. (eds.), *Gender and Health: An international perspective*, New Jersey, Prentice Hall.

Mazur, A., Booth, A. and Dabbs, J.M. (1992), 'Testosterone and chess competition', *Social Psychology Quarterly*, 55, 1, 70-77,

McCrea, F. and Markle, G. (1984), 'The estrogen replacement controversy in the USA and UK: Different answers to the same problem?', *Social Studies of Science*, 12,

McNay, L. (1992), *Foucault and Feminism: Power, Gender and the Self*, Boston, Northeastern University Press.

McNay, L. (1999), 'Gender, habitus and the field: Pierre Bourdieu and the limits of reflexivity', *Theory, Culture and Society*, 16, 1, 95-117,

Medvei, V.C. (1983), *A History of Endocrinology*, Lancaster, Boston, MTP Press.

Meinert, C.L. (1986), *Clinical Trials; Design, conduct, and analysis*, New York, Oxford, Oxford University Press.

Meldrum, M.L. (1994), 'Departures from the Design: The randomized clinical trial in historical context, 1946-1970', State University of New York at Stony Brook.

Merkatz, R.B., Temple, R., Sobel, S., Feiden, K. and Kessler, D.A. (1993), 'Women in clinical trials of new drugs: A change in Food and Drug Administration policy', *New England Journal of Medicine*, 329, 4, 292-96,

Merton, R.K. (1973), *The Sociology of Science*, Chicago and London, University of Chicago Press.

Money, J. (1988), *Gay, Straight, and In-Between: The sexology of erotic orientation*, New York, Oxford University Press.

Money, J. and Ehrhardt, A.A. (1972), *Man & Woman, Boy & Girl : The differentiation and dimorphism of gender identity from conception to maturity,* Baltimore, Johns Hopkins University Press.

Mosteller, F., Gilbert, J.P. and McPeek, B. (1983), 'Controversies in design and analysis of clinical trials', in Shapiro, S.H. and Louis, T.A. (eds.), *Clinical Trials: Issues and approaches,* New York, Basel, Marcel Dekker Inc.

Ms., (1994), July/August, 21, 'Update: Tamoxifen on trial', editorial.

Mulkay, M. (1979), *Science and the Sociology of Knowledge*, London, Allen & Unwin.

Naftolin, F. (1981), 'Understanding the bases of sex differences', *Science*, 211, 20 March,

Namer, M. (1996), 'Hormonotherapie des cancers du sein en phase metastatique chez les femmes menopausees', *Presse-Med*, 25, 35, 1745-53,

National Cancer Institute (1998), 'Questions and answers: The breast cancer prevention trial', http://207.121.187.155/NCI_TRIALS/zones/PressInfo/QuestionsAnswers/index.htm. last updated, 14.9.98, accessed February 1999..

Nayfield, S.G., Karp, J.E., Ford, L.G., Dorr, F.A. and Kramer, B.S. (1991), 'Potential role of tamoxifen in prevention of breast cancer', *Journal of the National Cancer Institute*, 83, 20, 1450-9,

Nelkin, D. (1987), *Selling Science: How the press covers science and technology*, New York, W. H. Freeman.

Newman, T.B., Browner, W.S., Cummings, S.R. and Hulley, S.B. (1988), 'Designing a new study: 2. Cross-sectional and case-control studies', in Hulley, S. and Cummings, S. (eds.), *Designing Clinical Research: An epidemiological approach*, Baltimore, Hong Kong, London, Sydney, Williams & Wilkins.

Nicholson, L.J. (ed.) (1990), *Feminism/Postmodernism*, Routledge, London, New York.

Nicholson, R.H. (1992), 'Prevention of breast cancer', *Lancet*, 340, 8834-8835, 1551-2,

Oakley, A. (1984), *The Captured Womb: A history of the medical care of pregnant women*, Oxford, Blackwell.

Oakley, A. (1989), 'Who's afraid of the randomized controlled trial? Some dilemmas of the scientific method and 'good' research practice', *Women and Health,* 15, 4, 25-59,

Oakley, A. (1991), 'Tamoxifen: In whose best interest?', *New Scientist*, 22 June,

Olby, R.C., Cantor, G.N., Christie, J.R.R. and Hodge, M.J.S. (1990), *Companion to the modern history of science*, London, Routledge.

Ortner, S.B. (1974), 'Is Female to Male as Nature is to Culture?', in Rosaldo, M.Z. and Lamphere, L. (eds.), *Women, Culture and Society*, Stanford, Standord University Press.

Oudshoorn, N. (1994), *Beyond the Natural Body: An archaeology of sex hormones*, London and New York, Routledge.

Pavlidis, N.A., Petris, C., Briassoulis, E., Klouvas, G., Psilas, C., Rempapis, J. and Petroutsos, G. (1992), 'Clear evidence that long-term, low-dose tamoxifen treatment can induce ocular toxicity', *Cancer*, 69, 2961-64,

Pearce, P.T., Myles, K.M. and Funder, J.W. (1993), 'Oestrogen and progesterone receptor assays in breast tumours; The Prince Henry's Hospital experience, 1983-1990', *Medical Journal of Australia*, 159, 16 August,

Petersen, A. and Lupton, D. (1996), *The New Public Health: Health and self in the age of risk,* Sydney, Allen & Unwin.

Petersen, A., and Bunton, R. (eds.), (1997), *Foucault: Health and Medicine*, London, New York, Routledge.

Petrow, V., Padilla, G.M., Mukherji, S. and Marts, S.A. (1984), 'Endocrine dependence of prostatic cancer upon dihydrotestosterone and not upon testosterone', *Journal of Pharmaceutical Pharmacology*, 36, 352-353,

Phoenix, C.H., Goy, R.W., Gerall, A.A. and Young, W.C. (1959), 'Organization action of testosterone propionate on the tissues mediating mating behaviors in the female guinea pig', *Endocrinology*, 65, 369-82,

Pickering, A. (1982), 'Interests and analogies', in Barnes, B. and Edge, D. (eds.), *Science in Context: Readings in the sociology of science*, Milton Keynes, The Open University Press.

Pinch, T. (1986), *Confronting Nature: The sociology of solar-neutrino detection*, Dordrecht, D Reidel.

Pineta, K.J., Replogle, T. and Lehr, J.E. (1995), 'Inhibition of prostate cancer growth by vinblastine and tamoxifen', *Prostate*, 26, 5, 270-274,

Pitts, J. (1968), 'Social control: The concept', in Sills, S.L. (ed.), *International Encyclopedia of the Social Sciences*, New York, Macmillan.

Placido, B., Griffin, J.E. and Wilson, J.D. (1990), 'Testosterone at high concentrations interacts with the human androgen receptor similarly to dihydrotestosterone', *Endocrinology*, 126, 2, 1165-1172,

Poovey, M. (1987), 'Scenes of an indelicate character: The medical 'treatment' of Victorian women', in Gallagher, C. and Laqueur, T. (eds.), *The Making of the Modern Body: Sexuality and society in the nineteenth century,* Berkely, University of California Press.

Popper, K.R. (1959), *The Logic of Scientific Discovery*, New York, Harper & Row.

Popper, K.R. (1963), *Conjectures and Refutations*, London, Routledge & Kegan Paul.

Porter, T. (1995), *Trust in Numbers: The pursuit of objectivity in science and public life*, Princeton, Princeton University Press.

Powles, T.J. (1992), 'The case for clinical trials of tamoxifen for prevention of breast cancer', *Lancet*, 340, 8828, 1145-7,

Powles, T.J., Hardy, J.R., Ashley, S.E., Farrington, G.M., Cosgrove, D., Davey, J.B., Dowsett, M., McKinna, J.A., Nash, A.G. and Sinnett, H.D. (1989), 'A pilot trial to evaluate the acute toxicity and feasibility of tamoxifen for prevention of breast cancer', *British Journal of Cancer*, 60, 1, 126-31,

Pritchard, K. (1998), 'Is tamoxifen effective in the prevention of breast cancer?', *Lancet*, 352, 80-81,

Raloff, J. (1992), 'Tamoxifen quandary: Promising cancer drug may hide a troubling dark side', *Science News*, 141, April 25, 266-269,

Ramazanoglu, C. (1992), 'What can you do with a man? Feminism and the critical appraisal of masculinity', *Women's Studies International Forum*, 15, 3, 339-350,

Reynolds, T. (1993), 'Prostate Cancer Prevention Trial Launched', *Journal of the National Cancer Institute*, 85, 20,

Richards, E. (1991), *Vitamin C and Cancer: Medicine or politics?,* London, Macmillian.

Riessman, C.K. (1992), 'Women and Medicalisation: A new perspective', in Kirkup, G. and Keller, L.S. (eds.), *Inventing Women: Science, technology and gender*, Cambridge, Polity Press.

Rimpela, A.H. and Pukkala, E.I. (1987), 'Cancers of affluence: Positive social class gradient and rising incidence trend in some cancer forms', *Social Science and Medicine*, 24, 601-606,

Ripper, M. (1991), 'The engendering of hormones: The role of the menstrual cycle and its disorders in the contemporary construction of gender', The Flinders University of South Australia.

Ripper, M. (1994), 'The engendering of hormonal difference', in Waddell, C. and Petersen, A.R. (eds.), *Just Health: Inequities in illness, care and prevention*, South Melbourne, Churchill Livingston.

Roman, P. (1988), 'The disease concept of alcoholism', *Drugs and Society*, 2, 5-32,

Rose, H. (1983), 'Hand, Brain and Heart: A feminist epistemology for the natural sciences', *Signs: Journal of Women in Culture and Society*, 9, 11, 73-90,

Rosenhan, D.L. (1973), 'On being sane in insane places', *Science*, 179, 250-58,

Ross, Bernstein and Judd (1976), 'Serum testosterone levels in young black and white men', *Journal of the National Cancer Institute*, 76, 45-48,

Ross, R.K., Coetzee, G.A., Reichardt, J., Skinner, E. and Henderson, B.E. (1995), 'Does the racial-ethnic variation in prostate cancer risk have a hormonal basis?', *Cancer (Supplement),* 75, 7,

Rossiter, M. (1982), *Women Scientists in America: Struggles and strategies to 1940,* Baltimore, Johns Hopkins University Press.

Russell, D. (1995), *Women, Madness and Medicine*, Cambridge, Polity Press.

Sabo, D. and Gordon, D. (1995), *Men's health and illness: Gender, power and the body*, London, Sage.

Saltman, D. (1994), 'Tamoxifen - triumph or torture?', *Healthsharing Women*, August-September,

Schatzkin, A., Paintadosi, S., Miccozzi, M. and Bartee, D. (1989), 'Alcohol consumption and breast cancer: A cross-national correlation study', International *Journal of Epidemiology*, 18, 1, 28-31,

Schiebinger, L. (1989), *The mind has no sex? Women in the origins of modern science*, Cambridge, London, Harvard University Press.

Scull, A.T. and Favreau, D. (1986), '"A chance to cut is a chance to cure": Sexual surgery for psychosis in three nineteenth century societies', *Research in Law Deviance and Social Control*, 8, 3-39,

Scully, D. (1980), *Men Who Control Women's Health: The miseducation of obstetrician-gynecologists*, Boston, Houghton Mifflin Company.

Seachrist, L. (1994), 'Restating the risks of tamoxifen', *Science*, 263, 910-911,

Segal, L. (1990, second edition 1997), *Slow motion: Changing masculinities, changing men*, London, Virago Press.

Shapin, S. and Schaffer, S. (1985), *Leviathan and the Air-Pump*, Princeton, Princeton University Press.

Shildrick, M. (1997), *Leaky bodies and boundaries: Feminism, postmodernism and (bio)ethics*, London, New York, Routledge.

Small, E.J. (1993), 'Prostate Cancer: Who to screen, and what the results mean', *Geriatrics*, 48, 12,

Smigel, K. (1991), 'Breast cancer prevention: Hold the hormones, please', *Journal of the National Cancer Institute*, 83, 17, 1211-3,

Smigel, K. (1992a), 'Breast cancer prevention trial takes off', *Journal of the National Cancer Institute*, 84, 9, 669-70,

Smigel, K. (1992b), 'Breast cancer prevention trial under scrutiny (again)', *Journal of the National Cancer Institute*, 84, 22, 1692-4,

Smigel, K. (1998), 'Breast cancer prevention trial shows major benefit, some risk', *Journal of the National Cancer Institute*, 90, 9, 647-648,

Smith, A. (1991), 'Women, consumer power and the health care system: Rocking the cradle is fine, just don't rock the boat', in Smith, A. (ed.), *Women's Health in Australia*, Armidale, University of New England Press.

Smith, D., Supramaniam, R., Coates, M. and Armstrong, B. (1998), 'Prostate Cancer in NSW in 1972 to 1994', NSW Cancer Council.

Smith, D.E. and David, S.J. (eds.) (1975), Women Look at Psychiatry, Press Gang Publishers, Vancouver.

Smith, W. and Broom, D. (1999), 'Can abortion trigger cancer?', Australian Doctor, June 18, 73,

Sontag, S. (1991), Illness as Metaphor & AIDS and its Metaphors, Middlesex England, Penguin Books.

Stevens, P.E. and Hall, J.M. (1991), 'A critical historical analysis of the medical construction of lesbianism', *International Journal of Health Services*, 21, 291-308,

Stoler, A. (1997), 'Educating desire in colonial Southeast Asia: Foucault, Freud and imperial sexualities', in Manderson, L. and Jolly, M. (eds.), *Sites of Desire, Economies of Pleasure: Sexualities in Asia and the Pacific*, Chicago

London, University of Chicago Press.

Szarka, C.E., Grana, G. and Engstrom, P.F. (1994), 'Chemoprevention of cancer', *Current Problems in Cancer*, 18, 1,

Szasz, T.S. (1961), *The Myth of Mental Illness*, New York, Harper & Row.

Szasz, T.S. (1970), *Manufacture of Madness: A comparative study of the inquisition and the mental health movement*, New York, Harper and Row.

Tacey, D. (1997), 'Masculinity, change and healing: Negotiating academic and popular perspectives on men's issues', in Huggins, A. (ed.), *Conference proceedings: Second National Men's Health Conference*, Perth, Curtin University of Technology.

Tiefer, L. (1995), *Sex is not a Natural Act: And other essays*, Boulder, San Francisco, Oxford, Westview Press.

Timmermans, S. and Berg, M. (1997), 'Standardization in action: Achieving local universality through medical protocols', *Social Studies of Science*, 27, 273-305,

Turken, S., Siris, E., Seldin, D., Flaster, E., Hyman, G. and Lindsay, R. (1989), 'Effects of tamoxifen on spinal bone density in women with breast cancer', *Journal of the National Cancer Institute*, 81, 14, 1086-8,

Turner, B.S. (1984), *The Body and Society*, Oxford, Basil Blackwell Inc.

Turner, B.S. (1992), *Regulating Bodies: Essays in medical sociology*, London and New York, Routledge.

Turner, B.S. (1997), 'Forward: From governmentality to risk, some reflections on Foucault's contribution to medical sociology', in Petersen, A., and Bunton, R. (eds) *Foucault: Health and Medicine*, London, New York, Routledge.

van den Wijngaard, M. (1997), *Reinventing the Sexes: The biomedical construction of femininity and masculinity*, Bloomington, Indianapolis, Indiana University Press.

van der Meijden, A.P.M. (1999), 'Practical aspects of clinical trials on chemoprevention of prostate cancer', *European Urology*, 35, 515-518,

van Leeuwen, F.E., Benraadt, J., Coebergh, J.W.W., Kiemney, L.A.L.M., Gimbrere, C.H.F., Otter, R., Schouten, L.J., Damhuis, R.A.M., Bontenbal, M., Diepenhorst, F.W., Belt-Dusebout, A.W.v.d. and Tinteren, H.v. (1994), 'Risk of endometrial cancer after tamoxifen treatment of breast cancer', *Lancet*, 343, February 19, 448-452,

Vanchieri, C. (1992), 'Breast cancer prevention study initiated in Italy', *Journal of the National Cancer Institute*, 84, 20, 1555-6,

Wajcman, J. (1991), *Feminism Confronts Technology*, Cambridge, Polity Press.

Waldby, C. (1996), *AIDs and the Body Politic: Biomedicine and sexual difference*, London and New York, Routledge.

Wasan, H.S. and Waxman, J. (1992), 'Hormonal management of prostate cancer', *Clinical Endocrinology*, 37,

Watney, S. (1990), 'Missionary Positions: AIDS, "Africa", and Race', *Differences: A Journal of Feminist Cultural Studies*, 1, 1, 83-99,

Wermeling, D.P. and Selwitz, A.D. (1993), 'Current issues surrounding women and minorities in drug trials', *The Annals of Pharmacotherapy*, 27, 7-8, 904-911,

White, J.W. (1893), 'The present position of the surgery of the hypertrophied prostate', *Annals of Surgery*, 18, 152-188,

White, K. and Willis, E. (1999), 'Positivism resurgent: The foundations of evidence based medicine', unpublished manuscript.

Wilson, B.E. and Reiner, W.G. (1998), 'Management of Intersex: A shifting paradigm', *Journal of Clinical Ethics*, 9, 4, 360-360,

Wilson, J., George, F. and Griffin, J. (1981), 'The hormonal control of sexual development', *Science*, 211, 20 March,

Wolter, J., Ryan, W.G. and Subbaiah, V. (1988), '(abstr 34)', Proc ASCO, 7, 10,

Worst Pills Best Pills newsletter (1998), 'Tamoxifen (Nolvadex) approved to reduce the risk of breast cancer', http://www.citizen.org/HRG/NEWSLETTER/pillsnews. accessed February 1999.

Young, I.M. (1990), *Throwing like a girl and other essays in feminist philosophy*, Bloomington, Indiana University Press.

Zeil, H. and Finkle, W. (1975), 'Increased risk of endometrial carcinoma among users of conjugated estrogens', *New England Journal of Medicine*, 293, 23,

Zola, I. (1983), *Socio-Medical Inquiries*, Philadelphia, Temple University Press.